	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L2	3239	("50" adj kda) or ("55" adj kda) or ("62" adj kda) or ("67" adj kda)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 11:59			0
2	BRS	L4	39	(cartilage adj oligomeric adj matrix adj protein) or (thrombospondin-5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:08			0
3	BRS	L5	0	2 same 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:05			0
4	BRS	L6	0	4 same trypsin same digest$3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:06			0
5	BRS	L7	17	hCOMP or (human adj cartilage adj oligomeric adj matrix adj protein) or (thrombospondin-5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:07			0
6	BRS	L8	35795	elisa	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:07			0
7	BRS	L10	0	8 same 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:08			0
8	BRS	L11	14	4 same (express$3 or recombinant)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:12			0
9	BRS	L12	2	4 same (express$3 or recombinant) same ca	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:14			0
10	BRS	L13	4	4 same (express$3 or recombinant) same calcium	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:15			0
11	BRS	L14	0	4 same purif$7 same calcium	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:16			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
12	BRS	L15	0	4 same purif$7 same edta	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:16			0
13	BRS	L16	7	4 same calcium	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:17			0
14	BRS	L17	126525	(biological adj matrix) or cartilage or (bone adj matrix) or collagen or hyaluronan or (fibrin adj gel) or (carbon adj fiber) or (polylactic adj acid)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:21			0
15	BRS	L18	39	4 same 17	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:22			0
16	BRS	L19	7	4 same 17 same calcium	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:24			0
17	BRS	L20	8	calcium-replete	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:25			0
18	BRS	L21	0	4 same 20	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:25			0
19	BRS	L22	5044	chondrocyte or (mesenchymal adj stem adj cell) or (differentiation adj agent) or (chondrocyte adj sulfate adj proteoglycan)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:29			0
20	BRS	L23	2	18 same 22	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/07 12:29			0

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FILE 'EMBASE' ENTERED AT 12:45:12 ON 07 JUN 2003
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FILE 'SCISEARCH' ENTERED AT 12:45:12 ON 07 JUN 2003
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FILE 'AGRICOLA' ENTERED AT 12:45:12 ON 07 JUN 2003

=> s (cartilage oligomeric matrix protein) or thrombospondin-5
L1        1010 (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5

=> s (50 kda) or (55 kda) or (62 kda) or (67 kda)
L2       35062 (50 KDA) OR (55 KDA) OR (62 KDA) OR (67 KDA)

=> s l1 (p) l2
L3           4 L1 (P) L2

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L3
L4            1 DUPLICATE REMOVE L3 (3 DUPLICATES REMOVED)

=> d l4 1 ibib abs

L4   ANSWER 1 OF 1     MEDLINE                    DUPLICATE 1
ACCESSION NUMBER:    93316223     MEDLINE
DOCUMENT NUMBER:     93316223   PubMed ID: 8326443
TITLE:               Sequential appearance of macromolecules in bone induction
                     in the rat.
AUTHOR:              Hulth A; Johnell O; Lindberg L; Heinegard D
CORPORATE SOURCE:    Department of Orthopaedics, General Hospital, University of
                     Lund, Malmo, Sweden.
SOURCE:              JOURNAL OF ORTHOPAEDIC RESEARCH, (1993 May) 11 (3) 367-78.
                     Journal code: 8404726. ISSN: 0736-0266.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals; Space Life Sciences
ENTRY MONTH:         199308
ENTRY DATE:          Entered STN: 19930820
                     Last Updated on STN: 19930820
                     Entered Medline: 19930806
AB   The appearance of noncollagenous proteins and proteoglycans during
     induction of cartilage and bone by implanted demineralized bone powder was
     studied by immunohistochemistry with polyclonal antibodies.  Three bone
     proteins (osteopontin, sialoprotein, and a   ***62***     ***kDa***
     protein) were present in the bone powder grains before implantation.  They
     appeared to be lost slowly from the granulation tissue but reappeared when
     bone formation started.  The raw powder also contained a cartilage
     protein, biglycan (S1), chondrocalcin,   ***cartilage***
       ***oligomeric***     ***matrix***     ***protein***  , and the large
     proteoglycan aggrecan.  The amounts of these molecules, however, increased
     significantly both within and outside the grains on cartilage formation.
     Cartilage matrix protein (148 kDa protein) appeared sparsely.  The 58 kDa
     protein and fibromodulin (59 kDa protein), particularly the latter, were
     prevalent in fibrillar bundles.  Antibodies against the laminin-staining
     vessel basement membranes showed an abundant occurrence of capillaries
     within the matrix grains in the granulation tissue and in the
     precartilaginous tissue.  Bone powder made noninductive by 4 M guanidine
     HCl did not induce cartilage and did not stain for antibodies against bone
     proteins or for molecules restricted to cartilage.


=> d his

     (FILE 'HOME' ENTERED AT 12:44:48 ON 07 JUN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     12:45:12 ON 07 JUN 2003
L1        1010 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5
L2       35062 S (50 KDA) OR (55 KDA) OR (62 KDA) OR (67 KDA)
L3           4 S L1 (P) L2
L4           1 DUPLICATE REMOVE L3 (3 DUPLICATES REMOVED)
```

```
=> s l4 (p) trypsin
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L25 (P) TRYPSIN'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L27 (P) TRYPSIN'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L29 (P) TRYPSIN'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L31 (P) TRYPSIN'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L33 (P) TRYPSIN'
L5            0 L4 (P) TRYPSIN

=> s hcomp or (human CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5
   4 FILES SEARCHED...
L6           85 HCOMP OR (HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOS
               PONDIN-5

=> s elisa
L7       261754 ELISA

=> s l7 and l1
L8           93 L7 AND L1

=> s l6 and l7
L9            6 L6 AND L7

=> duplicate remove l9
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L9
L10            2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)

=> d l10 1-2 ibib abs

L10  ANSWER 1 OF 2     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:    2003118858     IN-PROCESS
DOCUMENT NUMBER:     22446685   PubMed ID: 12559599
TITLE:               Monoclonal antibodies to   ***human***     ***cartilage***
                       ***oligomeric***     ***matrix***     ***protein***  :
                     epitope mapping and characterization of sandwich
                       ***ELISA***  .
AUTHOR:              Vilim Vladimir; Voburka Zdenek; Vytasek Richard; Senolt
                     Ladislav; Tchetverikov Ilja; Kraus Virginia B; Pavelka
                     Karel
CORPORATE SOURCE:    Institute of Rheumatology, Na Slupi 4, 128 50 Prague 2,
                     Czech Republic.. vili@revma.cz
CONTRACT NUMBER:     P60AG11268 (NIA)
SOURCE:              CLINICA CHIMICA ACTA, (2003 Feb) 328 (1-2) 59-69.
                     Journal code: 1302422. ISSN: 0009-8981.
PUB. COUNTRY:        Netherlands
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:          Entered STN: 20030314
                     Last Updated on STN: 20030314
AB   BACKGROUND: Cartilage oligomeric matrix protein/  ***thrombospondin***
       ***5***   (COMP/TSP 5) is one of the most promising serologic markers with
     regard to an ability to prognose development of osteoarthritis (OA).  Our
     aim was to map the epitopes of three monoclonal antibodies (mAb) to COMP
     and to develop and characterize a sandwich enzyme-linked immunosorbent
     assay (  ***ELISA***  ) for measuring COMP levels in human body fluids.
     METHODS: COMP was digested with trypsin and the NH(2)-terminal sequence of
     the fragments recognized by each of the mAbs was determined.  Steric
     competition among the mAbs was tested with an antibody capture assay.  A
     sandwich   ***ELISA***   was developed using unlabeled mAb 16-F12 as a
     capture antibody, and mAb 17-C10 labeled with biotin as the second
     antibody.  RESULTS: Epitopes of the three mAbs were mapped to three
     different domains within the COMP subunit (16-F12, NH(2)-terminal domain;
     17-C10, EGF-like domain; 12-C4, COOH-terminal domain).  These epitopes did
     not overlap. mAbs 17-C10 and 12-C4 yielded similar serum COMP results when
     used as the secondary antibodies.  Serum COMP levels measured with the new
     sandwich   ***ELISA***   using mAbs 16-F12 and 17-C10 correlated strongly
     with results based on an inhibition   ***ELISA***   with mAb 17-C10 alone
     (r(2) = 0.836; P < 0.0001).  We characterized the new sandwich
       ***ELISA***   with regards to inter- and intra-assay variability, the
     range of COMP levels that can be expected in human synovial fluids (SF)
```

and sera (controls and OA and rheumatoid arthritis (RA) patients), and the day-to-day and diurnal variability of COMP levels in sera. CONCLUSIONS: We have developed and characterized a sandwich ***ELISA*** for COMP that is sensitive and yields highly reproducible COMP results upon analysis of human sera and synovial fluids.

L10 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:373857 CAPLUS
DOCUMENT NUMBER: 136:84393
TITLE: Selection of peptides and synthesis of pentameric peptabody molecules reacting specifically with ErbB-2 receptor
AUTHOR(S): Houmel, Mehdi; Schneider, Pascal; Terskikh, Alexei; Mach, Jean-Pierre
CORPORATE SOURCE: Institute of Biochemistry, University of Lausanne, Lausanne, Switz.
SOURCE: International Journal of Cancer (2001), 92(5), 748-755
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The HER-2/ErbB-2 oncoprotein is overexpressed in human breast and ovarian adenocarcinomas and is clearly assocd. with the malignant phenotype. Although no specific ligand for this receptor has been pos. identified, ErbB-2 was shown to play a central role in a network of interactions with the related ErbB-1, ErbB-3 and ErbB-4 receptors. We have selected new peptides binding to ErbB-2 extracellular domain protein (ECD) by screening 2 newly developed constrained and unconstrained random hexapeptide phage libraries. Out of 37 phage clones, which bound specifically to ErbB-2 ECD, we found 6 constrained and 10 linear different hexapeptide sequences. Among the latter, 5 consensus motifs, all with a common methionine and a pos. charged residue at positions 1 and 3, resp., were identified. Furthermore, 3 representative hexapeptides were fused to a coiled-coil pentameric recombinant protein to form the so-called peptabodies recently developed in our lab. The 3 peptabodies bound specifically to the ErbB-2 ECD, as detd. by ***ELISA*** and BIA-core anal. and to tumor cells overexpressing ErbB-2, as shown by flow cytometry. Interestingly, one of the free selected linear peptides and all 3 peptabodies inhibited the proliferation of tumor cells overexpressing ErbB-2. In conclusion, a novel type of ErbB-2-specific ligand is described that might complement presently available monoclonal antibodies.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 12:44:48 ON 07 JUN 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 12:45:12 ON 07 JUN 2003
L1 1010 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5
L2 35062 S (50 KDA) OR (55 KDA) OR (62 KDA) OR (67 KDA)
L3 4 S L1 (P) L2
L4 1 DUPLICATE REMOVE L3 (3 DUPLICATES REMOVED)
L5 0 S L4 (P) TRYPSIN
L6 85 S HCOMP OR (HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROM
L7 261754 S ELISA
L8 93 S L7 AND L1
L9 6 S L6 AND L7
L10 2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)

=> s l1 (p) (express? or recombinant)
L11 286 L1 (P) (EXPRESS? OR RECOMBINANT)

=> s l11 (p) calcium
L12 28 L11 (P) CALCIUM

=> duplicate remove l12
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L12
L13 6 DUPLICATE REMOVE L12 (22 DUPLICATES REMOVED)

=> s l13 not (l4 or l10)
L14 6 L13 NOT (L4 OR L10)

=> d l14 1-6 ibib abs

L14 ANSWER 1 OF 6 MEDLINE
ACCESSION NUMBER: 2001196441 MEDLINE
DOCUMENT NUMBER: 21125809 PubMed ID: 11084047
TITLE: Mutations in cartilage oligomeric matrix protein causing pseudoachondroplasia and multiple epiphyseal dysplasia affect binding of calcium and collagen I, II, and IX.
AUTHOR: Thur J; Rosenberg K; Nitsche D P; Pihlajamaa T; Ala-Kokko L; Heinegard D; Paulsson M; Maurer P
CORPORATE SOURCE: Institute for Biochemistry, Medical Faculty, University of Cologne, D-50931 Koln, Germany.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Mar 2) 276 (9) 6083-92.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20030105
Entered Medline: 20010405

AB Mutations in type 3 repeats of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) cause two skeletal dysplasias, pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (MED). We ***expressed*** ***recombinant*** wild-type COMP that showed structural and functional properties identical to COMP isolated from cartilage. A fragment encompassing the eight type 3 repeats binds 14 ***calcium*** ions with moderate affinity and high cooperativity and presumably forms one large disulfide-bonded folding unit. A ***recombinant*** PSACH mutant COMP in which Asp-469 was deleted (D469 Delta) and a MED mutant COMP in which Asp-361 was substituted by Tyr (D361Y) were both secreted into the cell culture medium of human cells. Circular dichroism spectroscopy revealed only small changes in the secondary structures of D469 Delta and D361Y, demonstrating that the mutations do not dramatically affect the folding and stability of COMP. However, the local conformations of the type 3 repeats were disturbed, and the number of bound ***calcium*** ions was reduced to 10 and 8, respectively. In addition to collagen I and II, collagen IX also binds to COMP with high affinity. The PSACH and MED mutations reduce the binding to collagens I, II, and IX and result in an altered zinc dependence. These interactions may contribute to the development of the patient phenotypes and may explain why MED can also be caused by mutations in collagen IX genes.

L14 ANSWER 2 OF 6 MEDLINE
ACCESSION NUMBER: 2000464083 MEDLINE
DOCUMENT NUMBER: 20469946 PubMed ID: 11013461
TITLE: Delta 469 mutation in the type 3 repeat calcium binding domain of cartilage oligomeric matrix protein (COMP) disrupts calcium binding.
AUTHOR: Hou J; Putkey J A; Hecht J T
CORPORATE SOURCE: Department of Pediatrics, University of Texas Houston Medical School, Houston, USA.
SOURCE: CELL CALCIUM, (2000 Jun) 27 (6) 309-14.
Journal code: 8006226. ISSN: 0143-4160.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP/TSP5), a large glycoprotein found in the territorial matrix surrounding chondrocytes, is the fifth member of the thrombospondin (TSP) gene family. While the function of COMP is unknown, its importance is underscored by the finding that mutations in the highly conserved type 3 repeat domain causes two skeletal dysplasias. Pseudoachondroplasia (PSACH) and Multiple Epiphyseal Dysplasia, Fairbanks type (EDM1). The type 3 repeats are highly conserved low-affinity Ca(2+)binding domains that are found in all TSP genes. This study was undertaken to determine the effects of mutations on ***calcium*** binding and structure of the type 3 repeat domains. Wild-type (WT) and Delta469 ***recombinant***

COMP (rCOMP) proteins containing the entire ***calcium*** -binding domain were ***expressed*** in E. coli and purified. Equilibrium dialysis demonstrated that WT bound 10-12 Ca(2+)ions/molecule while Delta469 bound approximately half the Ca(2+)ions. Circular dichroism (CD) spectrometry had striking spectral changes for the WT in response to increasing concentrations of Ca(2+). These CD spectral changes were cooperative and reversible. In contrast, a large CD spectral change was not observed at any Ca(2+)concentration for Delta469. Moreover, both WT and Delta469 proteins produced similar CD spectral changes when titrated with Zn(2+), Cu(2+)and Ni(2+)indicating that the Delta469 mutation specifically affects only ***calcium*** binding. These results suggest that the Delta469 mutation, in the type 3 repeat region, interferes with Ca(2+)binding and that filling of all Ca(2+)binding loops may be critical for correct COMP protein conformation.

L14 ANSWER 3 OF 6 MEDLINE
ACCESSION NUMBER: 2000458618 MEDLINE
DOCUMENT NUMBER: 20409010 PubMed ID: 10852928
TITLE: Cartilage oligomeric matrix protein is a calcium-binding protein, and a mutation in its type 3 repeats causes conformational changes.
AUTHOR: Chen H; Deere M; Hecht J T; Lawler J
CORPORATE SOURCE: Division of Tumor Biology and Angiogenesis, Department of Pathology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts 02215, USA.
CONTRACT NUMBER: HL49081 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Aug 25) 275 (34) 26538-44.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000925

AB Mutations in residues in the type 3 ***calcium*** -binding repeats and COOH-terminal globular region of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) lead to two skeletal dysplasias, pseudoachondroplasia and multiple epiphyseal dysplasia. It has been hypothesized that these mutations cause COMP to misfold and to be retained in the endoplasmic reticulum. However, this hypothesis is not supported by previous reports that COMP, when purified in the presence of EDTA, shows no obvious difference in electron microscopic appearance in the presence or absence of ***calcium*** ions. Since this discrepancy may be due to the removal of ***calcium*** during purification, we have ***expressed*** wild-type COMP and the most common mutant form found in pseudoachondroplasia, MUT3, using a mammalian ***expression*** system and have purified both proteins in the presence of ***calcium*** . Both proteins are ***expressed*** as pentamers. Direct ***calcium*** binding experiments demonstrate that wild-type COMP, when purified in the presence of ***calcium*** , is a ***calcium*** -binding protein. Rotary shadowing electron microscopy and limited trypsin digestion at various ***calcium*** concentrations show that there are conformational changes associated with ***calcium*** binding to COMP. Whereas COMP exists in a more compact conformation in the presence of ***calcium*** , it shows a more extended conformation when ***calcium*** is removed. MUT3, with a single aspartic acid deletion in the type 3 repeats, binds less ***calcium*** and presents an intermediate conformation between the ***calcium*** -replete and ***calcium*** -depleted forms of COMP. In conclusion, we show that a single mutation in the type 3 repeats of COMP causes the mutant protein to misfold. Our data demonstrate the importance of ***calcium*** binding to the structure of COMP and provide a plausible explanation for the observation that mutations in the type 3 repeats and COOH-terminal globular region lead to pseudoachondroplasia.

L14 ANSWER 4 OF 6 MEDLINE
ACCESSION NUMBER: 2000219197 MEDLINE
DOCUMENT NUMBER: 20219197 PubMed ID: 10753957
TITLE: A cartilage oligomeric matrix protein mutation associated with pseudoachondroplasia changes the structural and functional properties of the type 3 domain.
AUTHOR: Maddox B K; Mokashi A; Keene D R; Bachinger H P
CORPORATE SOURCE: Research Department, Shriners Hospital for Children, Oregon

Health Sciences University, Portland, Oregon, 97201, USA.
CONTRACT NUMBER: AR45582 (NIAM[redacted]
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Apr 14) 275 (15) 11412-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000505

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) is a member of the thrombospondin family of extracellular matrix glycoproteins. All members of the family contain a highly conserved region of thrombospondin type 3 sequence repeats that bind ***calcium*** . A mutation in COMP previously identified in a patient with pseudoachondroplasia resulted in abnormal sequestration of COMP in distinctive rER vesicles. The mutation, Asp-446 --> Asn, is located in the type 3 repeats of the molecule. This region was ***expressed*** in a mammalian culture with and without the mutation to study the structural or functional properties associated with the mutation. The biophysical parameters of the mutant peptide were compared with those of the wild type and revealed the following difference: secondary structural analysis by circular dichroism showed more alpha-helix content in the wild-type peptides. The ***calcium*** binding properties of the two peptides were significantly different; there were 17 ***calcium*** ions bound/wild-type COMP3 peptide compared with 8/mutant peptide. In addition, wild-type COMP3 had a higher affinity for ***calcium*** and bound ***calcium*** more cooperatively. ***Calcium*** bound by the wild-type peptide was reflected in a structural change as indicted by velocity sedimentation. Thus, the effect of the COMP mutation appears to profoundly alter the ***calcium*** binding properties and may account for the difference observed in the structure of the type 3 domain. Furthermore, the highly cooperative binding of ***calcium*** to COMP3 suggests that these type 3 sequence repeats form a single protein domain, the thrombospondin type 3 domain.

L14 ANSWER 5 OF 6 MEDLINE
ACCESSION NUMBER: 1998420391 MEDLINE
DOCUMENT NUMBER: 98420391 PubMed ID: 9749943
TITLE: Characterization of cartilage oligomeric matrix protein (COMP) in human normal and pseudoachondroplasia musculoskeletal tissues.
AUTHOR: Hecht J T; Deere M; Putnam E; Cole W; Vertel B; Chen H; Lawler J
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical School at Houston, 77225, USA.
CONTRACT NUMBER: HL 49081 (NHLBI)
SOURCE: MATRIX BIOLOGY, (1998 Aug) 17 (4) 269-78.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981124

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), the fifth member of the -thrombospondin gene family, is an extracellular matrix ***calcium*** -binding protein. The importance of COMP is underscored by the finding that mutations in COMP cause the human dwarfing condition, pseudoachondroplasia (PSACH). Here, we report the results of human tissue distribution and cell secretion studies of human COMP. COMP is ***expressed*** and secreted by cultured monolayer chondrocyte, tendon and ligament cells, and COMP secretion is not restricted to a differentiated chondrocyte phenotype. Whereas COMP is retained in the endoplasmic reticulum that accumulates within PSACH chondrocytes in vivo, COMP is not retained intracellularly in the dedifferentiated PSACH chondrocytes in cultures. These results lend further support to the hypothesis that retention of COMP is related to the terminal PSACH chondrocyte phenotype, processing of proteins related to extracellular matrix formation, and maintenance in cartilage.

L14 ANSWER 6 OF 6 MEDLINE

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ACCESSION NUMBER:    93054522      MEDLINE
DOCUMENT NUMBER:     93054522    PubMed ID: 1429587
TITLE:               COMP (cartilage oligomeric matrix protein) is structurally
                     related to the thrombospondins.
AUTHOR:              Oldberg A; Antonsson P; Lindblom K; Heinegard D
CORPORATE SOURCE:    Department of Medical and Physiological Chemistry,
                     University of Lund, Sweden.
SOURCE:              JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Nov 5) 267 (31)
                     22346-50.
                     Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
OTHER SOURCE:        GENBANK-D12746; GENBANK-D12747; GENBANK-D12748;
                     GENBANK-D12749; GENBANK-D12750; GENBANK-D12751;
                     GENBANK-D12752; GENBANK-D12753; GENBANK-X72914;
                     GENBANK-Z14982
ENTRY MONTH:         199212
ENTRY DATE:          Entered STN: 19930122
                     Last Updated on STN: 19980206
                     Entered Medline: 19921201
AB   Cloning and sequence analysis of   ***cartilage***     ***oligomeric***
       ***matrix***     ***protein***   (COMP) cDNA, representing a cartilage
     pentameric protein, revealed a protein of 755 amino acid residues with a
     calculated molecular mass of 82,700 Da.    ***Expression***   of the cDNA
     in COS cells showed that COMP is a homopolymer composed of five identical
     disulfide-linked subunits.  COMP is homologous to the carboxyl-terminal
     half of thrombospondin, and the homologies include 89% and 54% of the
     residues in COMP and thrombospondin, respectively.  The similarities are
     most pronounced in the carboxyl-terminal domains and in the
       ***calcium***   binding type 3 repeat domains in which about 60% of the
     amino acid residues are identical.  In the type 2/epidermal growth factor
     repeat domains the two proteins contain 41% identical residues.  The
     sequence of the amino-terminal 84-amino acid residues is unique for COMP.
     Comparison of the amino acid sequences in the type 2 and type 3 repeat
     domains of COMP and the thrombospondins shows that COMP is the product of
     a unique gene and not the result of an alternatively spliced
     thrombospondin gene.


=> d his

     (FILE 'HOME' ENTERED AT 12:44:48 ON 07 JUN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     12:45:12 ON 07 JUN 2003
L1          1010 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5
L2         35062 S (50 KDA) OR (55 KDA) OR (62 KDA) OR (67 KDA)
L3             4 S L1 (P) L2
L4             1 DUPLICATE REMOVE L3 (3 DUPLICATES REMOVED)
L5             0 S L4 (P) TRYPSIN
L6            85 S HCOMP OR (HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROM
L7        261754 S ELISA
L8            93 S L7 AND L1
L9             6 S L6 AND L7
L10            2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)
L11          286 S L1 (P) (EXPRESS? OR RECOMBINANT)
L12           28 S L11 (P) CALCIUM
L13            6 DUPLICATE REMOVE L12 (22 DUPLICATES REMOVED)
L14            6 S L13 NOT (L4 OR L10)

=> s l1 (p) purif? (p) calcium
L15           10 L1 (P) PURIF? (P) CALCIUM

=> duplicate remove l15
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L15
L16            2 DUPLICATE REMOVE L15 (8 DUPLICATES REMOVED)

=> d l16 1-2 ibib abs

L16  ANSWER 1 OF 2     MEDLINE                                DUPLICATE 1
ACCESSION NUMBER:    2000458618      MEDLINE
DOCUMENT NUMBER:     20409010    PubMed ID: 10852928
TITLE:               Cartilage oligomeric matrix protein is a calcium-binding
```

protein, and a mutation in its type 3 repeats causes conformational changes.

AUTHOR: Chen H; Deere M; Hecht J T; Lawler J

CORPORATE SOURCE: Division of Tumor Biology and Angiogenesis, Department of Pathology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts 02215, USA.

CONTRACT NUMBER: HL49081 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Aug 25) 275 (34) 26538-44.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000925

AB Mutations in residues in the type 3 ***calcium*** -binding repeats and COOH-terminal globular region of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) lead to two skeletal dysplasias, pseudoachondroplasia and multiple epiphyseal dysplasia. It has been hypothesized that these mutations cause COMP to misfold and to be retained in the endoplasmic reticulum. However, this hypothesis is not supported by previous reports that COMP, when ***purified*** in the presence of EDTA, shows no obvious difference in electron microscopic appearance in the presence or absence of ***calcium*** ions. Since this discrepancy may be due to the removal of ***calcium*** during ***purification***, we have expressed wild-type COMP and the most common mutant form found in pseudoachondroplasia, MUT3, using a mammalian expression system and have ***purified*** both proteins in the presence of ***calcium***. Both proteins are expressed as pentamers. Direct ***calcium*** binding experiments demonstrate that wild-type COMP, when ***purified*** in the presence of ***calcium*** , is a ***calcium*** -binding protein. Rotary shadowing electron microscopy and limited trypsin digestion at various ***calcium*** concentrations show that there are conformational changes associated with ***calcium*** binding to COMP. Whereas COMP exists in a more compact conformation in the presence of ***calcium*** , it shows a more extended conformation when ***calcium*** is removed. MUT3, with a single aspartic acid deletion in the type 3 repeats, binds less ***calcium*** and presents an intermediate conformation between the ***calcium*** -replete and ***calcium*** -depleted forms of COMP. In conclusion, we show that a single mutation in the type 3 repeats of COMP causes the mutant protein to misfold. Our data demonstrate the importance of ***calcium*** binding to the structure of COMP and provide a plausible explanation for the observation that mutations in the type 3 repeats and COOH-terminal globular region lead to pseudoachondroplasia.

L16 ANSWER 2 OF 2 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 2000464083 MEDLINE
DOCUMENT NUMBER: 20469946 PubMed ID: 11013461

TITLE: Delta 469 mutation in the type 3 repeat calcium binding domain of cartilage oligomeric matrix protein (COMP) disrupts calcium binding.

AUTHOR: Hou J; Putkey J A; Hecht J T

CORPORATE SOURCE: Department of Pediatrics, University of Texas Houston Medical School, Houston, USA.

SOURCE: CELL CALCIUM, (2000 Jun) 27 (6) 309-14.
Journal code: 8006226. ISSN: 0143-4160.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP/TSP5), a large glycoprotein found in the territorial matrix surrounding chondrocytes, is the fifth member of the thrombospondin (TSP) gene family. While the function of COMP is unknown, its importance is underscored by the finding that mutations in the highly conserved type 3 repeat domain causes two skeletal dysplasias. Pseudoachondroplasia (PSACH) and Multiple Epiphyseal Dysplasia, Fairbanks type (EDM1). The type 3 repeats are highly conserved low-affinity Ca(2+)binding domains that are found in all TSP genes. This study was undertaken to determine

the effects of mutations on ***calcium*** binding and structure of the type 3 repeat domains. Wild type (WT) and Delta469 recombinant COMP (rCOMP) proteins containing the entire ***calcium*** -binding domain were expressed in E. coli and ***purified*** . Equilibrium dialysis demonstrated that WT bound 10-12 Ca(2+)ions/molecule while Delta469 bound approximately half the Ca(2+)ions. Circular dichroism (CD) spectrometry had striking spectral changes for the WT in response to increasing concentrations of Ca(2+). These CD spectral changes were cooperative and reversible. In contrast, a large CD spectral change was not observed at any Ca(2+)concentration for Delta469. Moreover, both WT and Delta469 proteins produced similar CD spectral changes when titrated with Zn(2+), Cu(2+)and Ni(2+)indicating that the Delta469 mutation specifically affects only ***calcium*** binding. These results suggest that the Delta469 mutation, in the type 3 repeat region, interferes with Ca(2+)binding and that filling of all Ca(2+)binding loops may be critical for correct COMP protein conformation.


```
=> s (biological matrix) or cartilage or (bone matrix) or collagen or hyaluronan or (fibrin gel) o
L17     634480 (BIOLOGICAL MATRIX) OR CARTILAGE OR (BONE MATRIX) OR COLLAGEN
               OR HYALURONAN OR (FIBRIN GEL) OR (CARBON FIBER) OR (POLYLACTIC
               ACID)

=> d his

     (FILE 'HOME' ENTERED AT 12:44:48 ON 07 JUN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     12:45:12 ON 07 JUN 2003
L1          1010 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5
L2         35062 S (50 KDA) OR (55 KDA) OR (62 KDA) OR (67 KDA)
L3             4 S L1 (P) L2
L4             1 DUPLICATE REMOVE L3 (3 DUPLICATES REMOVED)
L5             0 S L4 (P) TRYPSIN
L6            85 S HCOMP OR (HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROM
L7        261754 S ELISA
L8            93 S L7 AND L1
L9             6 S L6 AND L7
L10            2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)
L11          286 S L1 (P) (EXPRESS? OR RECOMBINANT)
L12           28 S L11 (P) CALCIUM
L13            6 DUPLICATE REMOVE L12 (22 DUPLICATES REMOVED)
L14            6 S L13 NOT (L4 OR L10)
L15           10 S L1 (P) PURIF? (P) CALCIUM
L16            2 DUPLICATE REMOVE L15 (8 DUPLICATES REMOVED)
L17       634480 S (BIOLOGICAL MATRIX) OR CARTILAGE OR (BONE MATRIX) OR COLLAGEN

=> s l1 (p) l17
L18        1001 L1 (P) L17

=> s l18 (p) composition
L19          19 L18 (P) COMPOSITION

=> duplicate remove l19
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L19
L20            8 DUPLICATE REMOVE L19 (11 DUPLICATES REMOVED)

=> d l20 1-8 ibib abs

L20  ANSWER 1 OF 8     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:    2002723012     IN-PROCESS
DOCUMENT NUMBER:     22373340   PubMed ID: 12485691
TITLE:               The influence of ageing and exercise on tendon growth and
                     degeneration-hypotheses for the initiation and prevention
                     of strain-induced tendinopathies.
AUTHOR:              Smith R K W; Birch H L; Goodman S; Heinegard D; Goodship A
                     E
CORPORATE SOURCE:    Department of Veterinary Clinical Sciences, The Royal
                     Veterinary College, Hawkshead Lane, North Mymms, Herts. AL9
                     7TA, Hatfield, UK.
SOURCE:              COMPARATIVE BIOCHEMISTRY AND PHYSIOLOGY. PART A, MOLECULAR
                     AND INTEGRATIVE PHYSIOLOGY, (2002 Dec) 133 (4) 1039-50.
                     Journal code: 9806096. ISSN: 1095-6433.
PUB. COUNTRY:        United States
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DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20021218
Last Updated on STN: 20021218

AB Strain-induced tendinopathy is a common injury in both human and equine athletes, with increasing incidence associated with greater involvement in sport and an increasingly aged population. This paper reviews our studies on the abundant non-collagenous protein, ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), in equine tendons. Its variation between tendon type and site, age and exercise has provided an insight into how age and exercise influence tendon growth and maturation. Tendons can be broadly divided into two types, reflecting their different matrix ***composition*** and function: the energy-storing tendons used for weight-bearing and locomotion, which suffer a high incidence of strain-induced tendinopathy, and positional tendons involved in limb placement or manipulative skills. It would appear that while energy-storing tendon can respond to the mechanical forces applied to it during growth, there is no evidence that it can do so after skeletal maturity. Instead, cumulative fatigue damage causes degeneration at the molecular level, potentially weakening it and increasing the risk of clinical injury. Appropriate exercise regimes early in life may help to improve the quality of growing tendon, thereby reducing the incidence of injury during ageing or subsequent athletic career.

L20 ANSWER 2 OF 8 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001011600 MEDLINE
DOCUMENT NUMBER: 20385047 PubMed ID: 10924396
TITLE: Differences in the concentration of various synovial fluid constituents between the distal interphalangeal joint, the metacarpophalangeal joint and the navicular bursa in normal horses.
AUTHOR: Viitanen M; Bird J; Maisi P; Smith R; Tulamo R M; May S
CORPORATE SOURCE: Farm Animal and Equine Medicine and Surgery, Royal Veterinary College, University of London, UK.
SOURCE: RESEARCH IN VETERINARY SCIENCE, (2000 Aug) 69 (1) 63-7. Journal code: 0401300. ISSN: 0034-5288.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001023

AB As a prerequisite for the identification of navicular disease markers, the concentrations of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), total glycosaminoglycans (GAG), ***hyaluronan*** , metalloproteinases (MMP) 2 and 9 and total protein were measured in synovial fluid samples obtained from the distal interphalangeal joint (DIP), the metacarpophalangeal joint (MCP) and the navicular bursa of 24 horses. Mean GAG, COMP and total protein levels were significantly higher in the DIP joint and in the navicular bursa compared to the MCP joint. ***Hyaluronan*** content was lower. MMP -2 activity was present in all fluids measured and had similar levels in different joints. MMP -9 was present in 42 per cent of MCP joint samples and 58 per cent of DIP joint samples and of navicular bursal samples. In relation to the constituents measured, the ***composition*** of navicular bursal fluid was similar to the articular synovial fluids, in particular that obtained from the DIP joint. Correlation between the constituents of DIP joint fluid and navicular bursal fluid obtained from the same legs was statistically significant for all the parameters measured.

L20 ANSWER 3 OF 8 MEDLINE
ACCESSION NUMBER: 2000124477 MEDLINE
DOCUMENT NUMBER: 20124477 PubMed ID: 10659252
TITLE: Should equine athletes commence training during skeletal development?: changes in tendon matrix associated with development, ageing, function and exercise.
AUTHOR: Smith R K; Birch H; Patterson-Kane J; Firth E C; Williams L; Cherdchutham W; van Weeren W R; Goodship A E
CORPORATE SOURCE: Royal Veterinary College, Hatfield, Herts, UK.
SOURCE: EQUINE VETERINARY JOURNAL. SUPPLEMENT, (1999 Jul) 30 201-9. Journal code: 9614088.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Jou s
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000302

AB In human athletes, conditioning, training and competition are commenced before skeletal maturity. Yet in equine athletics, racing of young (age 2 years) horses remains contentious. Tendon injury persists as major causes of wastage in equine athletes. Minimising injury and associated welfare issues could involve a radical approach to the timing and implementation of conditioning and training. Tendons were examined from Thoroughbreds, Dutch Warmblood foals, working horses and also a group of wild horses to evaluate effects of age, function and exercise. Gross mechanical properties did not differ significantly with age or exercise, but showed a high variance within each group. Mechanical properties of tendon tissue showed significant differences as a function of age and location. The ***collagen*** fibril crimp angle and length showed a regional reduction in the central core with exercise and age, with a synergistic effect. Regional differences in ***collagen*** fibril diameter were seen in long-term exercised older horses, but not in short-term exercised, or younger, horses. The higher proportion of small fibrils in the central region of the long-term exercised horses did not correlate with new ***collagen*** formation and therefore appear to result from disassembly of the larger diameter fibrils. Fibril diameter distributions were influenced by exercise regimens in the growing foal. Changes in molecular ***composition*** occurred in longer-term exercise and older horses, in the centre of the tendon, with higher levels of type III ***collagen*** and changes in glycosaminoglycan (GAG) content. ***Cartilage*** ***Oligomeric*** ***Matrix*** ***Protein*** (COMP) levels also appear to be modulated by age, function and superimposition of exercise. These changes were all exacerbated with age and exercise, suggesting appropriate exercise in young horses may lead to a lower incidence of injury than in older horses. An hypothesis is advanced that immature tendon can respond to exercise while mature tendon has limited, if any, ability to do so. These findings support potentially controversial earlier conditioning and racing of younger, rather than older, equine athletes.

L20 ANSWER 4 OF 8 MEDLINE
ACCESSION NUMBER: 2000447094 MEDLINE
DOCUMENT NUMBER: 20452295 PubMed ID: 10999666
TITLE: Age-related changes and effect of exercise on the molecular composition of immature equine superficial digital flexor tendons.
AUTHOR: Cherdchutham W; Becker C; Smith R K; Barneveld A; van Weeren P R
CORPORATE SOURCE: Department of Equine Sciences, Faculty of Veterinary Medicine, Utrecht University, The Netherlands.
SOURCE: EQUINE VETERINARY JOURNAL. SUPPLEMENT, (1999 Nov) (31) 86-94.
Journal code: 9614088.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001019

AB To test the hypothesis that exercise at very young age may influence the eventual molecular ***composition*** (and hence the biomechanical properties) of tendon tissue in the horse, 43 Dutch Warmblood foals were allotted to 3 differently exercised groups (box-rest, box-rest with training and pasture exercise). Twenty-four superficial digital flexor tendons (SDFTs) were collected at age 5 months (8 from each exercise group) and the others were obtained at 11 months after an additional period of light exercise that was equal for all remaining foals and was intended to see if any induced changes would be reversible or not. Significant changes in DNA content (cellularity), hyaluronic acid (HA) and polysulphated glycosaminoglycans (PSGAGs) were found after the 5 month period of different exercise regimens. There was a tendency towards an exercise-related effect on hydroxylysine content and number of hydroxylysylpyridinoline (HP) crosslinks. Levels of ***Cartilage*** ***Oligomeric*** ***Matrix*** ***Protein*** (COMP), measured by

homologous inhibition ELISA showed significant differences at 5 months and were highest in foals kept at pasture and lowest in foals maintained in a box but given enforced exercise. At 11 months, the biochemical parameters of the tendons from the foals of the former box-rest and pasture groups became similar, indicating the capacity of the immature tendon to recover from a retarded development. However, the ratio of PSGAGs per unit of DNA of the former training group was significantly lower than those from the other groups, suggesting that the training regimen in this study had a lasting negative effect on the tenocytes resulting in a decrease of the production of PSGAGs. Therefore, inappropriate or excessive exercise may damage developing tendon, with limited recovery after normalising the exercise level. These possibly deleterious effects of a training regimen on tendon development may be important for the management of young would-be equine athletes.

L20 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:706109 CAPLUS
DOCUMENT NUMBER: 129:285993
TITLE: Use of cartilage oligomeric matrix protein for the treatment of rheumatoid arthritis
INVENTOR(S): Heinegard, Dick; Lorentzen, Johnny C.; Klareskog, Lars
PATENT ASSIGNEE(S): Astra AB, Swed.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9846253	A1	19981022	WO 1998-SE682	19980414
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9870938	A1	19981111	AU 1998-70938	19980414
AU 746221	B2	20020418		
EE 9900464	A	20000417	EE 1999-464	19980414
BR 9808591	A	20000523	BR 1998-8591	19980414
EP 1019078	A1	20000719	EP 1998-917896	19980414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 338084	A	20010727	NZ 1998-338084	19980414
JP 2001520647	T2	20011030	JP 1998-543820	19980414
MX 9909288	A	20000331	MX 1999-9288	19991011
NO 9905004	A	19991014	NO 1999-5004	19991014
US 2001002392	A1	20010531	US 2000-750208	20001228

PRIORITY APPLN. INFO.: SE 1997-1409 A 19970415
WO 1998-SE682 W 19980414
US 1998-125937 A1 19980828

AB Use of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), or fragments or analogs thereof, for the manuf. of a pharmaceutical ***compn*** . for prevention or treatment of arthritic conditions is described, wherein the pharmaceutical ***compn*** . is administered in an amt. effective to prevent or treat the arthritic condition. The arthritogenicity of, and humoral reaction to, bovine COMP in rats is described.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 96:861470 SCISEARCH
THE GENUINE ARTICLE: VT565
TITLE: Patterns of glycosylation in ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** measured by monosaccharide ***composition*** analysis, MALDI/TOF and electrospray mass spectrometry
AUTHOR: Zaia J (Reprint); Boynton R; Heinegard D; Barry F
CORPORATE SOURCE: OSIRIS THERAPEUT INC, BALTIMORE, MD 21231
COUNTRY OF AUTHOR: USA
SOURCE: GLYCOBIOLOGY, (OCT 1996) Vol. 6, No. 7, pp. 115-115.
Publisher: OXFORD UNIV PRESS UNITED KINGDOM, WALTON ST

JOURNALS DEPT, OXFORD, ENGLAND OX2 6DP.
ISSN: 0959-6[redacted].
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 0

L20 ANSWER 7 OF 8 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 96195288 MEDLINE
DOCUMENT NUMBER: 96195288 PubMed ID: 8619919
TITLE: Predictors of joint damage in rheumatoid arthritis.
AUTHOR: Wollheim F A
CORPORATE SOURCE: Department of Rheumatology, Lund University Hospital, Sweden.
SOURCE: APMIS, (1996 Feb) 104 (2) 81-93. Ref: 103
Journal code: 8803400. ISSN: 0903-4641.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960627
Last Updated on STN: 19980206
Entered Medline: 19960614

AB Rheumatoid arthritis (RA) is the dominant form of destructive chronic arthritis with the potential to cause substantial disability and permanent functional impairment. The final extent and progression rate with time, however, varies markedly. In order to study effects of intervention and to support early aggressive and atoxic therapy in selected cases, predictive disease markers are needed. Recent advances regarding joint tissue ***composition*** and pathophysiology have defined a number of biological marker candidates which need to be explored for possible prognostic information. Some markers are characteristic for RA, such as rheumatoid factors and certain autoantibodies, which although they are more prevalent among patients with aggressive disease are not sensitive as predictors in early disease. Genetic susceptibility markers have been claimed to be good predictors of persisting arthritis in early synovitis clinics, but their role as severity markers in established disease is limited. Unspecific markers of inflammation, notably ESR or CRP when persistently elevated, are useful to monitor disease course and newer markers need to document their superiority over these. Another group of markers are attractive because of enriched or exclusive occurrence in joint tissue, and altered metabolism in joint disease. Thus, ***collagen*** type III propeptides, hyaluronates, and neopterin originating in the synovium could be useful, and, in particular, hyaluronate levels indeed do provide some predictive information. Highly tissue-specific ***cartilage*** metabolites include aggrecan fragments, ***collagen*** II fragments, ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) and the extraarticular ***cartilage*** matrix protein (CMP). When used alone or in combination in early disease some information can be obtained which may in the future facilitate prognostication. Bone metabolism can be monitored and there are different markers for synthesis and resorption. Meanwhile, whilst the new markers are essential research tools, their routine clinical usefulness remains to be proven.

L20 ANSWER 8 OF 8 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 93079835 MEDLINE
DOCUMENT NUMBER: 93079835 PubMed ID: 1448898
TITLE: Immunohistochemical localization of matrix proteins in the femoral joint cartilage of growing commercial pigs.
AUTHOR: Ekman S; Heinegard D
CORPORATE SOURCE: Department of Anatomy and Histology, Swedish University of Agricultural Sciences, Uppsala.
SOURCE: VETERINARY PATHOLOGY, (1992 Nov) 29 (6) 514-20.
Journal code: 0312020. ISSN: 0300-9858.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930129
Last Updated on STN: 19930129
Entered Medline: 19921228

AB The immunocytochemical localization of several matrix macromolecules,

including ***collagen*** type II and proteoglycans, in the distal femoral articular-epiphyseal ***cartilage*** complex of commercial pigs between the age of 6 and 18 weeks was studied. Early osteochondrotic lesions, i.e., chondronecrosis in the resting region of the growth ***cartilage*** , as well as extensions of necrotic ***cartilage*** into the subchondral bone, were present in all animals, except those 6 weeks old. A battery of antibodies were used for identification of macromolecules in the matrix at different stages of the disease. Chondrocyte involvement in the process could be studied by identifying the sequence of alterations in matrix macromolecules as the lesion developed. The immunostaining for aggrecan (large aggregating proteoglycans), ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** , fibronectin, ***collagen*** type II, fibromodulin, and biglycan was more prominent in the areas of chondronecrosis, extending into the subchondral bone, than in the normal resting region. This altered pattern of matrix macromolecules resembled that of the matrix of the proliferative chondrocytes and suggests that the chondrocyte maturation had stopped in the proliferative zone. The matrix in the areas of chondronecrosis in the resting region resembled that in the normal resting region. Thus the chondronecrosis appears to have preceded alterations of the matrix ***composition*** . The antibody reactivity pattern was, however, altered in the matrix of the clustered chondrocytes in areas of chondronecrosis. Staining in these regions suggested a more prominent appearance of fibronectin and ***collagen*** type II than in the normal matrix of the resting region. These changes are suggestive of attempt to repair. (ABSTRACT TRUNCATED AT 250 WORDS)

```
=> s calcium-replete
L21        140 CALCIUM-REPLETE

=> s l1 (p) l21
L22          5 L1 (P) L21

=> duplicate remove l22
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L22
L23            1 DUPLICATE REMOVE L22 (4 DUPLICATES REMOVED)

=> d l23 1 ibib abs

L23  ANSWER 1 OF 1     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:    2000458618     MEDLINE
DOCUMENT NUMBER:     20409010   PubMed ID: 10852928
TITLE:               Cartilage oligomeric matrix protein is a calcium-binding
                     protein, and a mutation in its type 3 repeats causes
                     conformational changes.
AUTHOR:              Chen H; Deere M; Hecht J T; Lawler J
CORPORATE SOURCE:    Division of Tumor Biology and Angiogenesis, Department of
                     Pathology, Beth Israel Deaconess Medical Center and Harvard
                     Medical School, Boston, Massachusetts 02215, USA.
CONTRACT NUMBER:     HL49081 (NHLBI)
SOURCE:              JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Aug 25) 275 (34)
                     26538-44.
                     Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200009
ENTRY DATE:          Entered STN: 20001005
                     Last Updated on STN: 20001005
                     Entered Medline: 20000925
AB   Mutations in residues in the type 3 calcium-binding repeats and
     COOH-terminal globular region of ***cartilage*** ***oligomeric***
     ***matrix*** ***protein*** (COMP) lead to two skeletal dysplasias,
     pseudoachondroplasia and multiple epiphyseal dysplasia. It has been
     hypothesized that these mutations cause COMP to misfold and to be retained
     in the endoplasmic reticulum. However, this hypothesis is not supported
     by previous reports that COMP, when purified in the presence of EDTA,
     shows no obvious difference in electron microscopic appearance in the
     presence or absence of calcium ions. Since this discrepancy may be due to
     the removal of calcium during purification, we have expressed wild-type
     COMP and the most common mutant form found in pseudoachondroplasia, MUT3,
     using a mammalian expression system and have purified both proteins in the
     presence of calcium. Both proteins are expressed as pentamers. Direct
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calcium binding experiments demonstrate that wild-type COMP, when purified in the presence of calcium, is a calcium-binding protein. Rotary shadowing electron microscopy and limited trypsin digestion at various calcium concentrations show that there are conformational changes associated with calcium binding to COMP. Whereas COMP exists in a more compact conformation in the presence of calcium, it shows a more extended conformation when calcium is removed. MUT3, with a single aspartic acid deletion in the type 3 repeats, binds less calcium and presents an intermediate conformation between the ***calcium*** - ***replete*** and calcium-depleted forms of COMP. In conclusion, we show that a single mutation in the type 3 repeats of COMP causes the mutant protein to misfold. Our data demonstrate the importance of calcium binding to the structure of COMP and provide a plausible explanation for the observation that mutations in the type 3 repeats and COOH-terminal globular region lead to pseudoachondroplasia.

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=> s chondrocyte or (mesenchymal stem cell) or (differentiation agent) or (chondrocyte sulfate pro
   4 FILES SEARCHED...
L24       49652 CHONDROCYTE OR (MESENCHYMAL STEM CELL) OR (DIFFERENTIATION AGENT
                ) OR (CHONDROCYTE SULFATE PROTEOGLYCAN)

=> d his

     (FILE 'HOME' ENTERED AT 12:44:48 ON 07 JUN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     12:45:12 ON 07 JUN 2003
L1          1010 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5
L2         35062 S (50 KDA) OR (55 KDA) OR (62 KDA) OR (67 KDA)
L3             4 S L1 (P) L2
L4             1 DUPLICATE REMOVE L3 (3 DUPLICATES REMOVED)
L5             0 S L4 (P) TRYPSIN
L6            85 S HCOMP OR (HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROM
L7        261754 S ELISA
L8            93 S L7 AND L1
L9             6 S L6 AND L7
L10            2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)
L11          286 S L1 (P) (EXPRESS? OR RECOMBINANT)
L12           28 S L11 (P) CALCIUM
L13            6 DUPLICATE REMOVE L12 (22 DUPLICATES REMOVED)
L14            6 S L13 NOT (L4 OR L10)
L15           10 S L1 (P) PURIF? (P) CALCIUM
L16            2 DUPLICATE REMOVE L15 (8 DUPLICATES REMOVED)
L17       634480 S (BIOLOGICAL MATRIX) OR CARTILAGE OR (BONE MATRIX) OR COLLAGEN
L18         1001 S L1 (P) L17
L19           19 S L18 (P) COMPOSITION
L20            8 DUPLICATE REMOVE L19 (11 DUPLICATES REMOVED)
L21          140 S CALCIUM-REPLETE
L22            5 S L1 (P) L21
L23            1 DUPLICATE REMOVE L22 (4 DUPLICATES REMOVED)
L24        49652 S CHONDROCYTE OR (MESENCHYMAL STEM CELL) OR (DIFFERENTIATION AG

=> s l18 (p) l24
L25          181 L18 (P) L24

=> duplicate remove l25
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L25
L26           45 DUPLICATE REMOVE L25 (136 DUPLICATES REMOVED)

=> d l26 1-45 ibib abs

L26  ANSWER 1 OF 45     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:    2003243202      IN-PROCESS
DOCUMENT NUMBER:     22650296   PubMed ID: 12766479
TITLE:               Apoptosis staining in cultured pseudoachondroplasia
                     chondrocytes.
AUTHOR:              Duke J; Montufar-Solis D; Underwood S; Lalani Z; Hecht J T
CORPORATE SOURCE:    Department of Orthodontics, Dental Branch, The University
                     of Texas Health Science Center at Houston..
                     Pauline.J.Duke@uth.tmc.edu
SOURCE:              APOPTOSIS, (2003 Mar) 8 (2) 191-7.
                     Journal code: 9712129. ISSN: 1360-8185.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
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LANGUAGE: English
FILE SEGMENT: IN-PROCESS; INDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030528
Last Updated on STN: 20030528

AB Pseudoachondroplasia (PSACH) is a skeletal dysplasia caused by a mutation in ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), a glycoprotein of normal ***cartilage*** matrix. PSACH ***chondrocytes*** have a distinctive phenotype with enlarged rER cisternae containing COMP, aggrecan, type IX ***collagen*** , and chaperone proteins. Ultrastructural studies suggested that this accumulation compromises cell function, hastening cell death, and consequently reducing the number of cells in the growth plate contributing to linear bone growth. Using the alginate bead system, we cultured control and PSACH ***chondrocytes*** for twenty weeks and one year to determine the effect of the mutation on size and number of ***cartilage*** nodules; and the presence of apoptotic cell death (TUNEL assay). At 20 weeks, beads containing PSACH or control ***chondrocytes*** did not differ in size and number of ***cartilage*** nodules or number of TUNEL-positive cells. After one year, nodule number, size and percent ***cartilage*** per bead were significantly less in PSACH nodules, and the number of cells staining positive for apoptosis was significantly greater than in controls (71.8% vs. 44.6%). The increase in apoptosis in PSACH nodules correlates with a decrease in growth of ***cartilage*** , supporting our hypothesis that death of damaged cells contributes to the growth plate defects in PSACH.

L26 ANSWER 2 OF 45 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2003059189 MEDLINE
DOCUMENT NUMBER: 22340650 PubMed ID: 12454393
TITLE: The mechanosensitivity of cartilage oligomeric matrix protein (COMP).
AUTHOR: Giannoni Paolo; Siegrist Mark; Hunziker Ernst B; Wong Marcy
CORPORATE SOURCE: M.E. Muller Institute for Biomechanics, University of Bern, Murtenstrasse 35, Postfach 30, 3010 Bern, Switzerland.
SOURCE: BIORHEOLOGY, (2003) 40 (1-3) 101-9.
Journal code: 0372526. ISSN: 0006-355X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030207
Last Updated on STN: 20030314
Entered Medline: 20030313

AB Physical forces are known to influence the synthesis, assembly and degradation of the ***cartilage*** extracellular matrix. The expression of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) was found to be sensitive to long term cyclic compression. Explants of calf articular ***cartilage*** as well as cylindrical alginate/ ***chondrocyte*** constructs were subjected to uniaxial unconfined dynamic compression for 18 hours after which total mRNA was extracted from samples. COMP expression was assessed by means of semi-quantitative RT-PCR and Northern blot techniques. The COMP transcript was found to be significantly enriched upon compression in both experimental systems. Incubation with anti-beta1 integrin blocking antibodies abolished the mechanosensitivity of COMP expression. In addition, the presence of a fully developed pericellular matrix was shown to be a prerequisite for enhanced COMP expression with cyclic loading. Cell/matrix interactions are therefore one of the key events in mechanotransduction in ***chondrocytes*** .

L26 ANSWER 3 OF 45 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:906677 CAPLUS
DOCUMENT NUMBER: 138:1975
TITLE: Method for establishing certification of chondrocytes
INVENTOR(S): Zheng, Ming Hao; Xu, Jiake
PATENT ASSIGNEE(S): Verigen Transplantation Service International, AG, Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002095399 A2 20021128 WO 2002-IB2752 20020329
W: AE, AG, AL, AM, AT, [redacted] AZ, BA, BB, BG, BR, BY, BZ, [redacted] CH, CN, CO, CR, CU, CZ, DE, [redacted] DM, DZ, EC, EE, ES, FI, GB, [redacted] GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-280242P P 20010330
AB The present invention provides a method for certifying cells for use in cartilage regeneration, the method comprising collecting data indicating chondrocyte cell viability for use in cartilage regeneration and providing a certificate of chondrocyte cell viability including the collecting data. A kit for quality assurance including instructions for collecting data indicating chondrocyte cell viability for use in cartilage regeneration and a certificate of chondrocyte cell viability is also included in the present invention. In addn., a method for detg. the likelihood of cartilage regeneration by assessing percent apoptosis in a chondrocyte cell culture is also provided.

L26 ANSWER 4 OF 45 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2002165697 MEDLINE
DOCUMENT NUMBER: 21895811 PubMed ID: 11782471
TITLE: Disease-causing mutations in cartilage oligomeric matrix protein cause an unstructured Ca2+ binding domain.
AUTHOR: Kleerekoper Quinn; Hecht Jacqueline T; Putkey John A
CORPORATE SOURCE: Department of Biochemistry, Structural Biology Research Center, University of Texas, Houston Medical School, Houston, Texas 77030, USA.
CONTRACT NUMBER: RO1HL45724 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Mar 22) 277 (12) 10581-9.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020319
Last Updated on STN: 20030105
Entered Medline: 20020429
AB ***Chondrocytes*** from pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (EDM1) patients display an enlarged rough endoplasmic reticulum that accumulates extracellular matrix proteins, including ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP). Mutations that cause PSACH and EDM1 are restricted to a 27-kDa Ca(2+) binding domain (type 3 repeat). This domain has 13 Ca(2+)-binding loops with a consensus sequence that conforms to Ca(2+)-binding loops found in EF hands. Most disease-causing mutations are found in the 11-kDa C-terminal region of this domain. We expressed recombinant native and mutant forms of the type 3 repeat domain (T3) and its 11-kDa C-terminal region (T3-Cterm). T3 and T3-Cterm bind approximately 13 and 8 mol of Ca(2+)/mol of protein, respectively. CD, one-dimensional proton, and two-dimensional (1)H-(15)N HSQC spectra of Ca(2+)-bound T3-Cterm indicate a distinct conformation that has little helical secondary structure, despite the presence of 13 EF hand Ca(2+)-binding loops. This conformation is also formed within the context of the intact T3. 19 cross-peaks found between 9.0 and 11.4 ppm are consistent with the presence of strong hydrogen bonding patterns, such as those in beta-sheets. Removal of Ca(2+) leads to an apparent loss of structure as evidenced by decreased dispersion and loss of all down field resonances. Deletion of Asp-470 (a mutation found in 22% of all PSACH and EDM1 patients) decreased the Ca(2+)-binding capacity of both T3 and T3-Cterm by about 3 mol of Ca(2+)/mol of protein. Two-dimensional (1)H-(15)N HSQC spectra of mutated T3-Cterm showed little evidence of defined structure in the presence or absence of Ca(2+). The data demonstrate that Ca(2+) is required to nucleate folding and to maintain defined structure. Mutation results in a partial loss of Ca(2+)-binding capacity and prevents Ca(2+)-dependent folding. Persistence of an unstructured state of the mutated Ca(2+) binding domain in COMP is the structural basis for retention of COMP in the rough endoplasmic reticulum of differentiated PSACH and EDM1 ***chondrocytes*** .

L26 ANSWER 5 OF 45 MEDLINE DUPLICATE 4

ACCESSION NUMBER: 2002717051 MEDLINE
DOCUMENT NUMBER: 22366901 PubMed ID: 12479386
TITLE: The murine COMP (cartilage oligomeric matrix protein) promoter contains a potent transcriptional repressor region.
AUTHOR: Han F; Kipnes J R; Li Y; Tuan R S; Hall D J
CORPORATE SOURCE: Cartilage Biology and Orthopaedics Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH, MSC 5755, Bldg 13, Rm 3W17, Bethesda, Maryland 20892, USA.
CONTRACT NUMBER: AR39740 (NIAMS)
AR45823 (NIAMS)
SOURCE: OSTEOARTHRITIS AND CARTILAGE, (2002 Aug) 10 (8) 638-45.
Journal code: 9305697. ISSN: 1063-4584.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021218
Last Updated on STN: 20030107
Entered Medline: 20030106

AB OBJECTIVE: A subgroup of patients with pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (MED) have been found to harbor mutations within the ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) gene. These two diseases are autosomal dominant disorders that are characterized by an early onset of osteoarthritis (OA). The COMP gene is expressed primarily in ***chondrocytes*** in articular ***cartilage*** as well as in tendon and ligament. Therefore, control over tissue specific COMP expression may be an important aspect in ***cartilage*** biology. To begin an analysis of the regulation of COMP expression, we have cloned, sequenced and characterized the entire genomic clone for mouse COMP that includes the COMP promoter. METHODS AND RESULTS: The COMP coding region spans 19 exons over approximately 8.4 kb of DNA. The arrangement and size of the exons have a remarkable similarity to those of the human COMP genomic sequence, indicating a significant degree of genomic conservation. Analysis of a 453 basepair region of the putative COMP promoter reveals two strong transcriptional repressor elements located between position -356 and -304 and between -251 and -180, relative to the start site for transcription. These repressor elements down-regulate transcription from the promoter in a broad spectrum of cell lines. Removal of the repressor DNA sequence from the COMP promoter leads to significant enhancement in transcriptional activity, indicating that this region acts in a dominant manner to transcriptional activators located more proximal to the start site of transcription. This region also represses transcription when linked to a heterologous promoter. CONCLUSIONS: This repressor region probably down-regulates transcription from the COMP promoter in vivo. It may help to repress transcription of COMP in non-cartilaginous tissues and/or may aid in the expression of COMP to the appropriate level in tissues such as ***cartilage*** , tendon and ligament.

L26 ANSWER 6 OF 45 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2002432171 MEDLINE
DOCUMENT NUMBER: 22176769 PubMed ID: 12189245
TITLE: Pseudoachondroplasia is caused through both intra- and extracellular pathogenic pathways.
AUTHOR: Dinser Robert; Zaucke Frank; Kreppel Florian; Hultenby Kjell; Kochanek Stefan; Paulsson Mats; Maurer Patrik
CORPORATE SOURCE: Institute for Biochemistry II, University of Cologne, Cologne, Germany.. robert.dinser@uniklinik-saarland.de
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (2002 Aug) 110 (4) 505-13.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020822
Last Updated on STN: 20020907
Entered Medline: 20020906

AB Pseudoachondroplasia is a dominantly inherited chondrodysplasia associated with mutations in ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP). Investigations into the pathogenesis of pseudoachondroplasia are hampered by its rarity. We developed a cell culture model by expressing mutant COMP in bovine primary

chondrocytes using a gutless adenoviral vector. We show that mutant COMP exerts its deleterious effects through both intra- and extracellular pathogenic pathways. Overexpression of mutant COMP led to a dose-dependent decrease in cellular viability. The secretion of mutant COMP was markedly delayed, presumably due to a prolonged association with chaperones in the endoplasmic reticulum (ER). The ECM lacked organized ***collagen*** fibers and showed amorphous aggregates formed by mutant COMP. Thus, pseudoachondroplasia appears to be an ER storage disease, most likely caused by improper folding of mutant COMP. The growth failure of affected patients may be explained by an increased cell death of growth-plate ***chondrocytes*** . Dominant interference of the mutant protein on ***collagen*** fiber assembly could contribute to the observed failure of the ECM of ***cartilage*** and tendons.

L26 ANSWER 7 OF 45 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2002466595 MEDLINE
DOCUMENT NUMBER: 22213800 PubMed ID: 12225811
TITLE: Matrix-matrix interaction of cartilage oligomeric matrix protein and fibronectin.
AUTHOR: Di Cesare Paul E; Chen Frank S; Moergelin Matthias; Carlson Cathy S; Leslie Michael P; Perris Roberto; Fang Carrie
CORPORATE SOURCE: Musculoskeletal Research Center, NYU-Hospital for Joint Diseases Department of Orthopedic Surgery, 301 East 17th Street, New York, NY 10030, USA.. pedicesare@aol.com
CONTRACT NUMBER: R01 AR45612-01A2 (NIAMS)
RR14099 (NCRR)
SOURCE: MATRIX BIOLOGY, (2002 Aug) 21 (5) 461-70.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20020913
Last Updated on STN: 20030325
Entered Medline: 20030324
AB Recent work indicates that ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) plays an important role in extracellular matrix assembly and matrix-matrix protein interactions. In order to identify the proteins in extracellular matrix that interact with COMP, we used an ELISA-based solid-phase binding assay, which revealed a specific, high-affinity interaction between COMP and fibronectin. This interaction is concentration-dependent and saturable, and appears to occur under physiologically relevant conditions. Electron microscopy after negative staining and fragment binding analysis using the solid-phase assay revealed a predominant binding site for the COMP C-terminal globular domain to a molecular domain approximately 14 nm from the N-terminal domain of fibronectin, which can be inhibited by the presence of a polyclonal antibody specific for the C-terminal heptadecapeptide of COMP. This interaction is further demonstrated in vivo by colocalization of both COMP and fibronectin in the ***chondrocyte*** pericellular matrix by laser confocal microscopy of ***chondrocytes*** grown in agarose culture, and by appositional and colocalization of these proteins in the growth plate of primates by immunohistochemistry.

L26 ANSWER 8 OF 45 CAPLUS
ACCESSION NUMBER: 2002:445175 CAPLUS
DOCUMENT NUMBER: 137:104160
TITLE: Molecular analysis of expansion, differentiation, and growth factor treatment of human chondrocytes identifies differentiation markers and growth-related genes
AUTHOR(S): Benz, Karin; Breit, Stephen; Lukoschek, Martin; Mau, Hans; Richter, Wiltrud
CORPORATE SOURCE: Department of Orthopaedic Surgery, University of Heidelberg, Heidelberg, 69118, Germany
SOURCE: Biochemical and Biophysical Research Communications (2002), 293(1), 284-292
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study is intended to optimize expansion and differentiation of cultured human chondrocytes by growth factor application and to identify mol. markers to monitor their differentiation state. The authors

dissected the mol. consequences of matrix release, monolayer, and 3D-alginate culture, growth factor optimized expansion, and re-differentiation protocols by gene expression anal. Among 19 common cartilage mols. assessed by cDNA array, six proved best to monitor differentiation. Instant down-regulation at release of cells from the matrix was strongest for COL 2A1, fibromodulin, and PRELP while LUM, CHI3L1, and CHI3L2 were expansion-related. Both gene sets reflected the physiol. effects of the most potent growth-inducing (PDGF-BB) and proteoglycan-inducing (BMP-4) factors. Only CRTAC1 expression correlated with 2D/3D switches while the mol. phenotype of native chondrocytes was not restored. The markers and optimized protocols the suggested can help to improve cell therapy of cartilage defects and chondrocyte differentiation from stem cell sources.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 9 OF 45 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003062945 EMBASE
TITLE: The mechanosensitivity of cartilage oligomeric matrix protein (COMP).
AUTHOR: Giannoni P.; Siegrist M.; Hunziker E.B.; Wong M.
CORPORATE SOURCE: M. Wong, M.E. Muller Inst. for Biomech., Murtenstrasse 35, 3010 Bern, Switzerland. wong@mem.unibe.ch
SOURCE: Biorheology, (2002) 40/1-3 (101-109).
Refs: 37
ISSN: 0006-355X CODEN: BRHLAU
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Physical forces are known to influence the synthesis, assembly and degradation of the ***cartilage*** extracellular matrix. The expression of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) was found to be sensitive to long term cyclic compression. Explants of calf articular ***cartilage*** as well as cylindrical alginate/ ***chondrocyte*** constructs were subjected to uniaxial unconfined dynamic compression for 18 hours after which total mRNA was extracted from samples. COMP expression was assessed by means of semi-quantitative RT-PCR and Northern blot techniques. The COMP transcript was found to be significantly enriched upon compression in both experimental systems. Incubation with anti-.beta.1 integrin blocking antibodies abolished the mechanosensitivity of COMP expression. In addition, the presence of a fully developed pericellular matrix was shown to be a prerequisite for enhanced COMP expression with cyclic loading. Cell/matrix interactions are therefore one of the key events in mechanotransduction in ***chondrocytes*** .

L26 ANSWER 10 OF 45 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2002092991 MEDLINE
DOCUMENT NUMBER: 21656885 PubMed ID: 11798989
TITLE: Autologous chondrocyte transplantation. Biomechanics and long-term durability.
AUTHOR: Peterson Lars; Brittberg Mats; Kiviranta Illka; Akerlund Evy Lundgren; Lindahl Anders
CORPORATE SOURCE: Gothenburg Medical Center, Gothenburg University, Gothenburg, Sweden.
SOURCE: AMERICAN JOURNAL OF SPORTS MEDICINE, (2002 Jan-Feb) 30 (1) 2-12.
Journal code: 7609541. ISSN: 0363-5465.
PUB. COUNTRY: United States
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020202
Last Updated on STN: 20020302
Entered Medline: 20020301
AB We evaluated the durability of autologous ***chondrocyte*** transplantation grafts in 61 patients treated for isolated ***cartilage*** defects on the femoral condyle or the patella and followed up for a mean of 7.4 years (range, 5 to 11). Durability was determined by comparing the clinical status at the long-term follow-up with that found 2 years after the transplantation. After 2 years, 50 of the 61 patients had good or excellent clinical results, and 51 of 61 had good or excellent results at 5 to 11 years later. Grafted areas from 11

of the patients were evaluated with an electromechanical indentation probe during a second-look arthroscopy procedure (mean follow-up, [redacted] months; range, 33 to 84); stiffness measurements were 90% or more of those of normal ***cartilage*** in eight patients. Eight of twelve 2-mm biopsy samples taken from these patients showed hyaline characteristics with safranin O staining and a homogeneous appearance in polarized light. Three fibrous and eight hyaline biopsy specimens stained positive to aggrecan and to ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** . Hyaline-like specimens stained positive for type II ***collagen*** , and fibrous, for type I ***collagen*** . Autologous ***chondrocyte*** transplantation for the treatment of articular ***cartilage*** injuries has a durable outcome for as long as 11 years.

L26 ANSWER 11 OF 45 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 2001322835 MEDLINE
DOCUMENT NUMBER: 21127441 PubMed ID: 11223338
TITLE: Analysis of the promoter region of human cartilage oligomeric matrix protein (COMP).
AUTHOR: Deere M; Rhoades Hall C; Gunning K B; LeFebvre V; Ridall A L; Hecht J T
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical School at Houston, Houston, TX 77030, USA.
CONTRACT NUMBER: CA16672 (NCI)
SOURCE: MATRIX BIOLOGY, (2001 Jan) 19 (8) 783-92.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF069520
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010611
Last Updated on STN: 20010611
Entered Medline: 20010607
AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) is an extracellular matrix protein expressed in ***cartilage*** , ligament, and tendon. The importance of COMP in the matrix of these cells is underscored by the discovery that mutations in COMP cause the skeletal dysplasias, pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (EDM1). Here, we present the first report on the analysis of the human COMP promoter region in ***cartilage*** , ligament, and tendon cells. A 1.7-kb region of the COMP promoter has been cloned and sequenced and no TATA or CAAT boxes were found. Primer extension identified multiple transcription start sites. All four transcription start sites were utilized in ***chondrocytes*** with only three of them utilized in tendon and ligament cells. Differential regulation was observed for different parts of this 1.7-kb region with the 370-bp proximal region conveying the strongest promoter activity. The highest activity was observed in tendon and ligament. Finally, we provide evidence that the DNA binding protein SP1 plays a role in the regulation of COMP expression. These results indicate that COMP expression within these cells is regulated in a unique manner that differs from the expression of other extracellular matrix genes.

L26 ANSWER 12 OF 45 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 2001640896 MEDLINE
DOCUMENT NUMBER: 21550102 PubMed ID: 11691584
TITLE: Selective intracellular retention of extracellular matrix proteins and chaperones associated with pseudoachondroplasia.
AUTHOR: Vranka J; Mokashi A; Keene D R; Tufa S; Corson G; Sussman M; Horton W A; Maddox K; Sakai L; Bachinger H P
CORPORATE SOURCE: Research Department, Shriners Hospital for Children, Portland, OR 97201, USA.
CONTRACT NUMBER: AR45582 (NIAMS)
SOURCE: MATRIX BIOLOGY, (2001 Nov) 20 (7) 439-50.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020205
Entered Medline: 20020204
AB Mutations in the ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) gene result in pseudoachondroplasia (PSACH), which

is a chondrodysplasia characterized by early-onset osteoarthritis and short stature. COMP is a secreted pentameric glycoprotein that belongs to the thrombospondin family of proteins. We have identified a novel missense mutation which substitutes a glycine for an aspartic acid residue in the thrombospondin (TSP) type 3 calcium-binding domain of COMP in a patient diagnosed with PSACH. Immunohistochemistry and immunoelectron microscopy both show abnormal retention of COMP within characteristically enlarged rER inclusions of PSACH ***chondrocytes*** , as well as retention of fibromodulin, decorin and types IX, XI and XII ***collagen*** . Aggrecan and types II and VI ***collagen*** were not retained intracellularly within the same cells. In addition to selective extracellular matrix components, the chaperones HSP47, protein disulfide isomerase (PDI) and calnexin were localized at elevated levels within the rER vesicles of PSACH ***chondrocytes*** , suggesting that they may play a role in the cellular retention of mutant COMP molecules. Whether the aberrant rER inclusions in PSACH ***chondrocytes*** are a direct consequence of chaperone-mediated retention of mutant COMP or are otherwise due to selective intracellular protein interactions, which may in turn lead to aggregation within the rER, is unclear. However, our data demonstrate that retention of mutant COMP molecules results in the selective retention of ECM molecules and molecular chaperones, indicating the existence of distinct secretory pathways or ER-sorting mechanisms for matrix molecules, a process mediated by their association with various molecular chaperones.

L26 ANSWER 13 OF 45 MEDLINE DUPLICATE 10

ACCESSION NUMBER: 2002026731 MEDLINE
DOCUMENT NUMBER: 21363816 PubMed ID: 11470401
TITLE: Calreticulin, PDI, Grp94 and BiP chaperone proteins are associated with retained COMP in pseudoachondroplasia chondrocytes.
AUTHOR: Hecht J T; Hayes E; Snuggs M; Decker G; Montufar-Solis D; Doege K; Mwalle F; Poole R; Stevens J; Duke P J
CORPORATE SOURCE: University of Texas Medical School at Houston, Department of Pediatrics, P.O. Box 20708, Houston, TX 77225-0708, USA.. jacqueline.t.hecht@uth.tmc.edu
SOURCE: MATRIX BIOLOGY, (2001 Jul) 20 (4) 251-62. Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020131
Entered Medline: 20011207

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), a large pentameric glycoprotein and member of the thrombospondin (TSP) group of extracellular proteins, is found in the territorial matrix surrounding ***chondrocytes*** . More than 50 unique COMP mutations have been identified as causing two skeletal dysplasias: pseudoachondroplasia (PSACH); and multiple epiphyseal dysplasia (EDM1). Recent studies suggest that calcium-binding and calcium-induced protein folding differ between wild type and mutant proteins, and abnormal processing of the mutant COMP protein contributes to the characteristic enlarged lamellar appearing rER cisternae in PSACH and EDMI ***chondrocytes*** in vivo and in vitro. Towards the goal of delineating the pathogenesis of PSACH and EDM1, in-vivo PSACH growth plate and in-vitro PSACH ***chondrocytes*** cultured in alginate beads were examined to identify and localize the chaperone proteins participating in the processing of the retained extracellular matrix proteins in the PSACH rER. Aggrecan was localized to both the rER cisternae and matrix while COMP and type IX ***collagen*** were only found in the rER. Type II ***collagen*** was solely found in the ECM suggesting that it is processed and transported differently from other retained ECM proteins. Five chaperone proteins: BiP (Grp78); calreticulin (CRT); protein disulfide (PDI); ERp72; and Grp94, demonstrated immunoreactivity in the enlarged PSACH cisternae and the short rER channels of ***chondrocytes*** from both in-vivo and in-vitro samples. The chaperone proteins cluster around the electron dense material within the enlarged rER cisternae. CRT, PDI and GRP94 AB-gold particles appear to be closely associated with COMP. Immunoprecipitation and Western blot, and Fluorescence Resonance Energy Transfer (FRET) analyses indicate that CRT, PDI and GRP94 are in close proximity to normal and mutant COMP and BiP to mutant COMP. These results suggest that these proteins play a role in the processing and transport of wild type COMP in normal ***chondrocytes*** and in the retention of mutant COMP in PSACH ***chondrocytes*** .

L26 ANSWER 14 OF 45 MEDLINE DUPLICATE

ACCESSION NUMBER: 2001431622 MEDLINE
DOCUMENT NUMBER: 21372013 PubMed ID: 11478845
TITLE: Chondrogenic differentiation of mesenchymal stem cells from bone marrow: differentiation-dependent gene expression of matrix components.
AUTHOR: Barry F; Boynton R E; Liu B; Murphy J M
CORPORATE SOURCE: Osiris Therapeutics, Inc., 2001 Aliceanna Street, Baltimore, Maryland 21231, USA.. fbarry@osiristx.com
SOURCE: EXPERIMENTAL CELL RESEARCH, (2001 Aug 15) 268 (2) 189-200. Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010924
Last Updated on STN: 20010924
Entered Medline: 20010920

AB Transforming growth factor (TGF)-beta-induced chondrogenesis of ***mesenchymal*** ***stem*** ***cells*** derived from bone marrow involves the rapid deposition of a ***cartilage*** -specific extracellular matrix. The sequential events in this pathway leading from the undifferentiated stem cell to a mature ***chondrocyte*** were investigated by analysis of key matrix elements. Differentiation was rapidly induced in cells cultured in the presence of TGF-beta 3 or -beta 2 and was accompanied by the early expression of fibromodulin and ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** . An increase in aggrecan and versican core protein synthesis defined an intermediate stage, which also involved the small leucine-rich proteoglycans decorin and biglycan. This was followed by the appearance of type II ***collagen*** and chondroadherin. The pathway was also characterized by the appearance of type X ***collagen*** , usually associated with hypertrophic ***cartilage*** . There was also a change in the pattern of sulfation of chondroitin sulfate, with a progressive increase in the proportion of 6-sulfated species. The major proportion of newly synthesized glycosaminoglycan was part of an aggregating proteoglycan network. These data allow us to define the phenotype of the differentiated cell and to understand in greater detail the sequential process of matrix assembly.

L26 ANSWER 15 OF 45 MEDLINE DUPLICATE 12

ACCESSION NUMBER: 2001349628 MEDLINE
DOCUMENT NUMBER: 21305865 PubMed ID: 11412822
TITLE: Cartilage and bone biological markers in the synovial fluid of osteoarthritic patients after hyaluronan injections in the knee.
AUTHOR: Herrero-Beaumont G; Guerrero R; Sanchez-Pernaute O; Acebes C; Palacios I; Mas S; Rodriguez I; Egido J; Vivanco F
CORPORATE SOURCE: Inflammation Research Unit, Fundacion Jimenez Diaz, Avda. Reyes Catolicos 2, 28040 Madrid, Spain.. gherrero@fjd.es
SOURCE: CLINICA CHIMICA ACTA, (2001 Jun) 308 (1-2) 107-15. Journal code: 1302422. ISSN: 0009-8981.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010730
Last Updated on STN: 20010730
Entered Medline: 20010726

AB OBJECTIVE: To evaluate synovial fluid levels of ***cartilage*** and bone biological markers after repetitive intra-articular injections of sodium hyaluronate (HA) in knee osteoarthritis (OA) patients. METHODS: Twenty patients with knee OA were evaluated before and after 5 weekly injections of HA. To study ***cartilage*** and bone biological markers, synovial fluid and urine samples were collected simultaneously with the first (FI=week 0) and before the last injection (LI=week 4) of HA. Not commercially available markers (***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), proteoglycan monomers and cyanogen bromide peptide 11 of the type II ***collagen*** chains (alpha (II) CA11B)) were determined by an indirect inhibition ELISA developed and standardized in our laboratory. RESULTS: We found a significant reduction in levels of proteoglycan monomers (30+/-16 vs.

22+/-10 microg/ml, p<0.05), an increase in COMP concentration (2.9+/-0.9 vs. 3.6+/-0.9 microg/ml, p<0.05) and osteocalcin (BGP) level (8.7+/-8 vs. 11.9+/-9 ng/ml, p<0.05). No significant changes were observed in the levels of alpha (II)CB11B), metalloproteinase-1 (MMP-1) or pyridinium cross-link/creatinine (Pyr/Cr). CONCLUSIONS: HA could elicit an indirect response on the ***cartilage*** and bone metabolism due to the increased overuse of the joint caused by the analgesic effect of HA. However, a direct HA action on the metabolism of ***chondrocytes*** must not be ruled out.

L26 ANSWER 16 OF 45 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 2001439865 MEDLINE
DOCUMENT NUMBER: 21378166 PubMed ID: 11485547
TITLE: ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) and ***collagen*** IX are sensitive markers for the differentiation state of articular primary ***chondrocytes*** .
AUTHOR: Zaucke F; Dinser R; Maurer P; Paulsson M
CORPORATE SOURCE: Institute for Biochemistry II, Medical Faculty, University of Cologne, Joseph-Stelzmann-Strasse 52, D-50931 Cologne, Germany.. frank.zaucke@uni-koeln.de
SOURCE: BIOCHEMICAL JOURNAL, (2001 Aug 15) 358 (Pt 1) 17-24. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010924
Last Updated on STN: 20010924
Entered Medline: 20010920

AB Primary ***chondrocytes*** dedifferentiate in serial monolayer with respect to their morphological and biosynthetic phenotype. They change from a round to a flattened fibroblast-like shape, and ***collagen*** I is secreted instead of the ***cartilage*** -specific ***collagen*** II. We analysed in detail the time course of dedifferentiation of mature bovine articular ***chondrocytes*** in monolayer for up to 32 weeks. Assessment of RNA expression by reverse transcription-PCR led to the identification of two novel phenotypical markers, the ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) and ***collagen*** IX, which are down-regulated faster than the widely accepted marker, ***collagen*** II. The different kinetics of COMP and ***collagen*** expression suggest differential regulation at the level of transcription. Immunostaining and metabolic labelling experiments confirmed the switch in the ***collagen*** expression pattern and the rapid down-regulation of de novo synthesis of COMP and ***collagen*** IX. Culture of ***chondrocytes*** in a three-dimensional matrix is known to stabilize the chondrocytic phenotype. We maintained cells for up to 28 weeks in an alginate bead system, which prevented dedifferentiation and led to a stabilization of ***collagen*** and COMP expression. Immunohistochemical analysis of the alginate beads revealed a similar distribution of matrix proteins to that found in vivo. ***Chondrocytes*** were transferred after a variable length of monolayer culture into the alginate matrix and the potential for redifferentiation was investigated. The re-expression of COMP and ***collagen*** IX was differentially regulated. The expression of COMP was re-induced within days after transfer into the three-dimensional matrix, while the expression of ***collagen*** IX was irreversibly down-regulated. In summary, these results demonstrate that the potential for redifferentiation decreases with increasing length of monolayer culture and show that the alginate bead system represents an attractive in vitro model to study the ***chondrocyte*** de- and re-differentiation processes, as well as extracellular matrix assembly.

L26 ANSWER 17 OF 45 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 2000122597 MEDLINE
DOCUMENT NUMBER: 20122597 PubMed ID: 10655510
TITLE: A mutation in the alpha 3 chain of type IX collagen causes autosomal dominant multiple epiphyseal dysplasia with mild myopathy.
AUTHOR: Bonnemann C G; Cox G F; Shapiro F; Wu J J; Feener C A; Thompson T G; Anthony D C; Eyre D R; Darras B T; Kunkel L M
CORPORATE SOURCE: Department of Medicine (Genetics), Children's Hospital, Boston, MA 02115, USA.
CONTRACT NUMBER: P30-HD18655 (NICHD)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2000 Feb 1) 97 (3) 1212-7.

Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United State[redacted]
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000302

AB Multiple epiphyseal dysplasia (MED) is a degenerative ***cartilage*** condition shown in some cases to be caused by mutations in genes encoding ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** or type IX ***collagen*** . We studied a family with autosomal dominant MED affecting predominantly the knee joints and a mild proximal myopathy. Genetic linkage to the COL9A3 locus on chromosome 20q13.3 was established with a peak log(10) odds ratio for linkage score of 3.87 for markers D20S93 and D20S164. Reverse transcription-PCR performed on the muscle biopsy revealed aberrant mRNA lacking exon 3, which predicted a protein lacking 12 amino acids from the COL3 domain of alpha3(IX) ***collagen*** . Direct sequencing of genomic DNA confirmed the presence of a splice acceptor mutation in intron 2 of the COL9A3 gene (intervening sequence 2, G-A, -1) only in affected family members. By electron microscopy, ***chondrocytes*** from epiphyseal ***cartilage*** exhibited dilated rough endoplasmic reticulum containing linear lamellae of alternating electron-dense and electron-lucent material, reflecting abnormal processing of mutant protein. Type IX ***collagen*** chains appeared normal in size and quantity but showed defective cross-linking by Western blotting. The novel phenotype of MED and mild myopathy is likely caused by a dominant-negative effect of the exon 3-skipping mutation in the COL9A3 gene. Patients with MED and a waddling gait but minimal radiographic hip involvement should be evaluated for a primary myopathy and a mutation in type IX ***collagen*** .

L26 ANSWER 18 OF 45 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 2001070110 MEDLINE
DOCUMENT NUMBER: 21003353 PubMed ID: 11117291
TITLE: Expression of cartilage oligomeric matrix protein (COMP) by embryonic and adult osteoblasts.
AUTHOR: Di Cesare P E; Fang C; Leslie M P; Tulli H; Perris R; Carlson C S
CORPORATE SOURCE: Musculoskeletal Research Center, Hospital for Joint Diseases Orthopaedic Institute, New York, New York 10003, USA.. pedicesare@aol.com
CONTRACT NUMBER: RO1-RR14099 (NCRR)
SOURCE: JOURNAL OF ORTHOPAEDIC RESEARCH, (2000 Sep) 18 (5) 713-20.
Journal code: 8404726. ISSN: 0736-0266.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010104

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** has been implicated as an important component of endochondral ossification because of its direct effects on ***chondrocytes*** . The importance of this protein for skeletal development and growth has been recently illustrated by the identification of mutations in ***cartilage*** oligomeric protein genes in two types of inherited chondrodysplasias and osteoarthritic phenotypes: multiple epiphyseal dysplasia and pseudoachondroplasia. In the present study, we report the presence of ***cartilage*** oligomeric protein in embryonic and adult osteoblasts. A foot from a 21-week-old human fetus, subchondral bone obtained from knee replacement surgery in an adult patient, and a limb from a 19-day-postcoital mouse embryo were analyzed with immunostaining and in situ hybridization. In the human fetal foot, ***cartilage*** oligomeric protein was localized to osteoblasts of the bone collar and at the newly formed bone at the growth plate and bone diaphyses. Immunostaining was performed on the adult subchondral bone and showed positive intracellular staining for ***cartilage*** oligomeric protein of the osteoblasts lining the trabecular bone. There was no staining of the osteocytes. Immunostaining of the mouse limb showed the most intense staining for ***cartilage*** oligomeric protein in the hypertrophic ***chondrocytes*** and in the surrounding osteoblast cells of the developing bone. ***Cartilage*** oligomeric protein mRNA and protein were detected in an osteoblast cell line (MG-63), and ***cartilage***

oligomeric protein mRNA was detected from human cancellous bone RNA. These results suggest that altered structure of ***cartilage*** oligomeric protein by the mutations seen in pseudoachondroplasia and multiple epiphyseal dysplasia may have direct effects on osteoblasts, contributing to the pathogenesis of these genetic disorders.

L26 ANSWER 19 OF 45 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 2000397422 MEDLINE
DOCUMENT NUMBER: 20391398 PubMed ID: 10937619
TITLE: Chondrocyte-specific enhancer regions in the COMP gene.
AUTHOR: Issack P S; Fang C; Leslie M P; Di Cesare P E
CORPORATE SOURCE: Musculoskeletal Research Center, Department of Orthopaedic Surgery, New York University Medical Center-Hospital for Joint Diseases, New York 10003, USA.
SOURCE: JOURNAL OF ORTHOPAEDIC RESEARCH, (2000 May) 18 (3) 345-50. Journal code: 8404726. ISSN: 0736-0266.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000817

AB The molecular events governing the differentiation of mesenchymal cells into ***chondrocytes*** and the expression of ***cartilage*** marker genes are poorly understood. ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** is a noncollagenous extracellular matrix protein with a relatively ***cartilage*** -specific spatial and temporal expression pattern. To understand the mechanisms controlling ***chondrocyte*** -specific expression of ***cartilage*** ***oligomeric*** ***matrix*** ***protein***, we cloned 1.9 kb of the 5' flanking promoter sequence of the murine ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** gene and identified two spatially distant ***cartilage*** -specific enhancer regions by deletion analysis. One element is situated proximally (proximal positive element: -125 to -75) and a second region is located distally (distal positive region: -1925 to -592) relative to the transcription start site. Interestingly, nucleotides within the proximal positive element are conserved between the mouse and human promoters and resemble consensus sites for the binding of members of the high mobility group class of transcription factors. Defining ***cartilage*** -specific regulatory elements in the ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** promoter may provide useful molecular probes for identifying transcription factors that control acquisition of the chondrocytic phenotype.

L26 ANSWER 20 OF 45 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 2000464083 MEDLINE
DOCUMENT NUMBER: 20469946 PubMed ID: 11013461
TITLE: Delta 469 mutation in the type 3 repeat calcium binding domain of cartilage oligomeric matrix protein (COMP) disrupts calcium binding.
AUTHOR: Hou J; Putkey J A; Hecht J T
CORPORATE SOURCE: Department of Pediatrics, University of Texas Houston Medical School, Houston, USA.
SOURCE: CELL CALCIUM, (2000 Jun) 27 (6) 309-14. Journal code: 8006226. ISSN: 0143-4160.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP/TSP5), a large glycoprotein found in the territorial matrix surrounding ***chondrocytes*** , is the fifth member of the thrombospondin (TSP) gene family. While the function of COMP is unknown, its importance is underscored by the finding that mutations in the highly conserved type 3 repeat domain causes two skeletal dysplasias. Pseudoachondroplasia (PSACH) and Multiple Epiphyseal Dysplasia, Fairbanks type (EDM1). The type 3 repeats are highly conserved low-affinity Ca(2+)binding domains that are found in all TSP genes. This study was undertaken to determine the effects of mutations on calcium binding and structure of the type 3 repeat domains. Wild-type (WT) and Delta469

recombinant COMP (rCOMP) proteins containing the entire calcium-binding domain were expressed in E. coli and purified. Equilibrium dialysis demonstrated that WT bound 10-12 Ca(2+)ions/molecule while Delta469 bound approximately half the Ca(2+)ions. Circular dichroism (CD) spectrometry had striking spectral changes for the WT in response to increasing concentrations of Ca(2+). These CD spectral changes were cooperative and reversible. In contrast, a large CD spectral change was not observed at any Ca(2+)concentration for Delta469. Moreover, both WT and Delta469 proteins produced similar CD spectral changes when titrated with Zn(2+), Cu(2+)and Ni(2+)indicating that the Delta469 mutation specifically affects only calcium binding. These results suggest that the Delta469 mutation, in the type 3 repeat region, interferes with Ca(2+)binding and that filling of all Ca(2+)binding loops may be critical for correct COMP protein conformation.

L26 ANSWER 21 OF 45 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 2000068043 MEDLINE
DOCUMENT NUMBER: 20068043 PubMed ID: 10601736
TITLE: Distribution of cartilage molecules in the developing mouse joint.
AUTHOR: Murphy J M; Heinegard R; McIntosh A; Sterchi D; Barry F P
CORPORATE SOURCE: Osiris Therapeutics Inc., Baltimore, MD 21231, USA.
SOURCE: MATRIX BIOLOGY, (1999 Oct) 18 (5) 487-97.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000218
Entered Medline: 20000210

AB This study describes the precise spatial and temporal patterns of protein distribution for aggrecan, fibromodulin, ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) and ***cartilage*** matrix protein (CMP) in the developing mouse limb with particular attention to those cells destined to form articular ***chondrocytes*** in comparison to those cells destined to form a mineralized tissue and become replaced by bone. Mouse glenohumeral joints from fetal mice (12-18 days post coitus (dpc) to the young adult (37 days after birth) were immunostained with antibodies specific for these molecules. Aggrecan staining defined the general chondrocytic phenotype, whether articular or transient. Fibromodulin was associated with prechondrocytic mesenchymal cells in the interzone prior to joint cavitation and with the mesenchymal cells of the perichondrium or the periosteum encapsulating the joint elements of the maturing and young adult limb. Staining was most intense around developing articular ***chondrocytes*** and much less abundant or absent in those differentiating cells along the anlage. CMP showed an almost reciprocal staining pattern to fibromodulin and was not detected in the matrix surrounding articular ***chondrocytes*** . COMP was not detected in the cells at the articular surface prior to cavitation but by 18 dpc, as coordinated movement of the mouse forelimb intensifies, staining for COMP was most intense around the maturing articular ***chondrocytes*** . These results show that the cells that differentiate into articular ***chondrocytes*** elaborate an extracellular matrix distinct from those cells that are destined to form bone. Fibromodulin may function in the early genesis of articular ***cartilage*** and COMP may be associated with elaboration of a weight-bearing ***chondrocyte*** matrix.

L26 ANSWER 22 OF 45 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 1999303228 MEDLINE
DOCUMENT NUMBER: 99303228 PubMed ID: 10376735
TITLE: Localization and expression of cartilage oligomeric matrix protein by human rheumatoid and osteoarthritic synovium and cartilage.
AUTHOR: Di Cesare P E; Fang C; Leslie M P; Della Valle C J; Gold J M; Tulli H; Perris R; Carlson C S
CORPORATE SOURCE: Musculoskeletal Research Center, Department of Orthopaedic Surgery, New York University Medical Center-Hospital for Joint Diseases, New York 10003, USA.. PEDiCesare@aol.com
CONTRACT NUMBER: RR08562 (NCRR)
SOURCE: JOURNAL OF ORTHOPAEDIC RESEARCH, (1999 May) 17 (3) 437-45.
Journal code: 8404726. ISSN: 0736-0266.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Jou s
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990714
Last Updated on STN: 19990714
Entered Medline: 19990630

AB Synovium and ***cartilage*** from patients with osteoarthritis or rheumatoid arthritis were analyzed for expression of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** . Immunostaining of synovium with antiserum to ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** demonstrated positive staining in both diseases. In osteoarthritis, there was positive staining within the synovial cells and immediately subjacent connective tissue, with less intense staining in the deeper connective tissue. In rheumatoid arthritis, there was less intense staining within the synovial cells and marked intense staining in the deeper connective tissue. In situ hybridization performed with an antisense digoxigenin-labeled riboprobe to human ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** confirmed the presence of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** mRNA in the cells of the synovial lining in both types of synovium. Quantitative polymerase chain reaction with a ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** MIMIC demonstrated increased ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** mRNA in rheumatoid ***cartilage*** and synovium as compared with osteoarthritic ***cartilage*** and synovium, respectively; mRNA levels in rheumatoid synovium were similar to those from osteoarthritic ***chondrocytes*** . As a result of the high expression of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** from rheumatoid synovium, inflammatory synovium should be considered as a potential tissue source of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** in any investigation of biological markers of ***cartilage*** metabolism. The upregulated expression of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** in inflammatory tissues suggests its in vivo regulation by cytokines.

L26 ANSWER 23 OF 45 MEDLINE DUPLICATE 20
ACCESSION NUMBER: 1999444774 MEDLINE
DOCUMENT NUMBER: 99444774 PubMed ID: 10517186
TITLE: Cyclic compression of articular cartilage explants is associated with progressive consolidation and altered expression pattern of extracellular matrix proteins.
AUTHOR: Wong M; Siegrist M; Cao X
CORPORATE SOURCE: M.E. Muller Institute for Biomechanics, Bern, Switzerland.. wong@mem.unibe.ch
SOURCE: MATRIX BIOLOGY, (1999 Aug) 18 (4) 391-9.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991103

AB In this study, we investigated the biosynthetic response of full thickness, adult bovine articular ***cartilage*** explants to 45 h of static and cyclic unconfined compression. The cyclic compression of articular ***cartilage*** resulted in a progressive consolidation of the ***cartilage*** matrix. The oscillatory loading increased protein synthesis ([35S]methionine incorporation) by as much as 50% above free swelling control values, but had an inhibitory influence on proteoglycan synthesis ([35SO4] incorporation). As expected, static compression was associated with a dose-dependent decrease in biosynthetic activity. ECM oligomeric proteins which were most affected by mechanical loading were fibronectin and ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP). Static compression at all amplitudes caused a significant increase in fibronectin synthesis over free swelling control levels. Cyclic compression of articular ***cartilage*** at 0.1 Hz and higher was consistently associated with a dramatic increase in the synthesis of COMP as well as fibronectin. The biosynthetic activity of ***chondrocytes*** appears to be sensitive to both the frequency and amplitude of the applied load. The results of this study support the hypothesis that ***cartilage*** tissue can remodel its extracellular matrix in response to alterations in functional demand.

L26 ANSWER 24 OF 45 MEDLINE DUPLICATE 21

ACCESSION NUMBER: 1999105925 MEDLINE
DOCUMENT NUMBER: 99105925 PubMed ID: 9887340
TITLE: Trinucleotide expansion mutations in the cartilage oligomeric matrix protein (COMP) gene.
AUTHOR: Delot E; King L M; Briggs M D; Wilcox W R; Cohn D H
CORPORATE SOURCE: Ahmanson Department of Pediatrics, Steven Spielberg Pediatric Research Center, Burns and Allen Cedars-Sinai Research Institute, and Department of Pediatrics, UCLA School of Medicine, Los Angeles, CA 90048, USA.
CONTRACT NUMBER: AR43139 (NIAMS)
SOURCE: HUMAN MOLECULAR GENETICS, (1999 Jan) 8 (1) 123-8. Journal code: 9208958. ISSN: 0964-6906.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990326
Last Updated on STN: 19990326
Entered Medline: 19990318

AB Pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (MED) are two human autosomal dominant skeletal dysplasias characterized by variable short stature, joint laxity and early-onset degenerative joint disease. Both disorders can result from mut-ations in the gene for ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), an extracellular matrix glycoprotein. About one-third of PSACH cases result from heterozygosity for deletion of one codon within a very short triplet repeat, (GAC)5, which encodes five consecutive aspartic acid residues within the calmodulin-like region of the COMP protein. We have identified two expansion mut-ations in this repeat: an MED patient carrying a (GAC)6allele and a PSACH patient carrying a (GAC)7allele. These are among the shortest disease-causing triplet repeat expansion mutations described thus far, and are the first identified in a GAC repeat. A unique feature of this sequence is that expansion as well as shortening of the repeat can cause the same disease. In ***cartilage*** , both patients have rough endoplasmic reticulum inclusions in ***chondrocytes*** . The inclusions are also present in tendon tissue and can be reproduced in cultured tendon cells, suggesting that the pathophysiology of disease is similar in both ***cartilage*** and tendon.

L26 ANSWER 25 OF 45 MEDLINE
ACCESSION NUMBER: 2000304130 MEDLINE
DOCUMENT NUMBER: 20304130 PubMed ID: 10847517
TITLE: Pseudoachondroplastic dysplasia: an Iowa review from human to mouse.
AUTHOR: Stevens J W
CORPORATE SOURCE: Department of Orthopaedic Surgery, The University of Iowa, Iowa City 52242-1181, USA.. jeff-stevens@uiowa.edu
SOURCE: IOWA ORTHOPAEDIC JOURNAL, (1999) 19 53-65. Ref: 68
Journal code: 8908272.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000720
Last Updated on STN: 20000720
Entered Medline: 20000713

AB Lamellar inclusions of the rough endoplasmic reticulum in growth plate ***chondrocytes*** , first identified (1972) in the Department of Orthopaedic Surgery, University of Iowa, has become the cytochemical hallmark for the pseudoachondroplastic dysplasia (PSACH) phenotype, linking an endoplasmic reticulum storage disorder with the osteochondrodysplasia. Since this original observation, great advances have been made, leading to the molecular understanding of this altered longitudinal bone growth anomaly. A PSACH canine model suggested that abatement of cumulative vertical growth of growth plate ***chondrocytes*** seen in PSACH results from (1) altered extracellular matrix constraints for horizontal growth and (2) uncoupling of endochondral and perichondral growth that causes metaphyseal flaring. PSACH, an autosomal dominant disease, is linked to mutation of the ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) gene. Amino acid substitutions, deletions, or additions is proposed to alter COMP structure that cause its retention in the rough

endoplasmic reticulum of growth plate ***chondrocytes*** , leading to (1) compositional and structural change of the extracellular matrix, and (2) altered cellular proliferation and volume expansion. Normal growth and development occurs in COMP gene knockout mice that do not synthesis COMP, demonstrating that a mutant COMP, not absence of COMP, is required for the PSACH phenotype. The mechanism by which mutant COMP induces a PSACH phenotype remains to be elucidated. At the University of Iowa a cell culture system has been developed whereby mutant COMP transgenes are introduced into ***chondrocytes*** and the expressed product COMP is retained in the endoplasmic reticulum. This readily manipulated system makes it possible to decipher systematically the system's cellular secretory processing pathway, in order to clarify the mechanism(s) by which the mutant COMP is retained within the endoplasmic reticulum. Concurrent with this is the development of transgenic mice expressing the mutant COMP used in the cell culture system. This will make it possible to establish that expression of a human PSACH-linked mutant COMP will produce a PSACH phenotype. A PSACH animal model will provide a means to characterize the mechanism of altered longitudinal bone growth and to test gene therapy approaches for correcting the anomaly.

L26 ANSWER 26 OF 45 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 1998434583 MEDLINE
DOCUMENT NUMBER: 98434583 PubMed ID: 9756911
TITLE: Physiological and pathological secretion of cartilage oligomeric matrix protein by cells in culture.
AUTHOR: Delot E; Brodie S G; King L M; Wilcox W R; Cohn D H
CORPORATE SOURCE: Ahmanson Department of Pediatrics, Steven Spielberg Pediatric Research Center, Burns, Allen Cedars-Sinai Research Institute, and Departmentof Pediatrics, UCLA School of Medicine, Los Angeles, CA 90048, USA.
CONTRACT NUMBER: AR43139 (NIAMS)
HD22567 (NICHD)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Oct 9) 273 (41) 26692-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981102
AB Abnormalities in ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), a pentameric structural protein of the ***cartilage*** extracellular matrix, have been identified in pseudoachondroplasia and multiple epiphyseal dysplasia, two human autosomal dominant osteochondrodysplasias. However, the function of the protein remains unknown. With the goal of establishing a model to study the mechanisms by which COMP mutations cause disease, we have analyzed synthesis and secretion of COMP in cultured ***chondrocytes*** , tendon, and ligament cells. Pentameric protein detected inside of control cells suggested that pentamerization is an intracellular process. Patient cells expressed mutant and normal RNA and secreted COMP at levels similar to controls, suggesting that abnormal pentamers are likely to be found in the extracellular matrix. Inclusions within patient ***cartilage*** stained with anti-COMP antibodies, and cultured cells presented similar inclusions, indicating that presumably abnormal COMP pentamers are less efficiently secreted than normal molecules. We conclude that the COMP disorders are likely to result from a combination of a decreased amount of COMP in the matrix and a dominant negative effect due to the presence of abnormal pentamers in ***cartilage*** .

L26 ANSWER 27 OF 45 MEDLINE DUPLICATE 23
ACCESSION NUMBER: 1998288698 MEDLINE
DOCUMENT NUMBER: 98288698 PubMed ID: 9627009
TITLE: Regulation of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** synthesis in human synovial cells and articular ***chondrocytes*** .
AUTHOR: Recklies A D; Baillargeon L; White C
CORPORATE SOURCE: Shriners Hospital for Children and McGill University, Montreal, Quebec, Canada.
SOURCE: ARTHRITIS AND RHEUMATISM, (1998 Jun) 41 (6) 997-1006.
Journal code: 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980716
Last Updated on STN: 19980716
Entered Medline: 19980707

AB OBJECTIVE: ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) is a component of the extracellular matrix of articular ***cartilage*** . Its increased presence in synovial fluid and serum has been associated with accelerated joint damage in patients with rheumatoid arthritis (RA) and osteoarthritis. To fully understand the reasons for fluctuations of COMP levels, we studied the biosynthesis of this molecule in cells derived from joint tissues. METHODS: Synovial cells were derived from synovial tissues of patients with RA, and human articular ***chondrocytes*** were prepared from normal articular ***cartilage*** . Analysis by Northern blotting was used to evaluate steady-state levels of COMP messenger RNA (mRNA), while secretion of the protein into culture media was analyzed by Western blotting. Expression of COMP in synovial tissues was studied by reverse transcriptase-polymerase chain reaction analysis and by in situ hybridization. RESULTS: COMP was synthesized and secreted by synovial cells as well as by articular ***chondrocytes*** in culture. The basal rate of synthesis was very low; however, COMP biosynthesis in both cell populations was induced very strongly by transforming growth factor beta1 (TGFbeta1). Interleukin-1beta counteracted COMP induction by TGF-beta1. COMP was not detected in culture media of skin or fetal lung fibroblasts, either in the absence or the presence of TGFbeta1. COMP mRNA was also present in fresh synovial tissue specimens obtained from patients with RA. CONCLUSION: COMP is synthesized and secreted not only by articular ***chondrocytes*** , but also by synovial fibroblasts. The demonstration of COMP expression in surgical specimens of synovial tissues suggests that the inflamed synovium may provide an additional source for the elevated levels of COMP observed in arthritis. Thus, increased COMP levels in body fluids may be indicative of active synovitis as well as of accelerated joint erosion.

L26 ANSWER 28 OF 45 MEDLINE DUPLICATE 24
ACCESSION NUMBER: 1998378148 MEDLINE
DOCUMENT NUMBER: 98378148 PubMed ID: 9714346
TITLE: Analysis of cartilage oligomeric matrix protein (COMP) in synovial fibroblasts and synovial fluids.
AUTHOR: Hummel K M; Neidhart M; Vilim V; Hauser N; Aicher W K; Gay R E; Gay S; Hauselmann H J
CORPORATE SOURCE: Center for Experimental Rheumatology, University Hospital, Zurich, Switzerland.
SOURCE: BRITISH JOURNAL OF RHEUMATOLOGY, (1998 Jul) 37 (7) 721-8. Journal code: 8302415. ISSN: 0263-7103.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980904

AB We investigated the expression of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) in normal and rheumatoid arthritis (RA) synovial fibroblasts. In situ hybridization (ISH) was conducted on synovial specimens from five RA patients applying specific probes for COMP or fibroblast ***collagen*** type I. ISH was combined with immunohistochemistry, applying antibodies to the macrophage marker CD68. Ribonuclease protection assay (RPA) and rapid amplification of 3'-cDNA ends (3'-RACE) were performed on total RNA from normal and RA synovial fibroblast cultures. Protein extracts from fibroblasts and culture supernatants were compared with synovial fluids and protein extracts from isolated ***chondrocytes*** by Western blot utilizing polyclonal and monoclonal antibodies (18-G3 mAb) to COMP. COMP mRNA was detected in fibroblasts of RA synovium by ISH, and in normal and RA synovial fibroblast cultures by RPA. 3'-RACE demonstrated sequence homology of ***chondrocyte*** and synovial fibroblast COMP along the coding sequence. COMP protein was detected in synovial fibroblasts and culture supernatants by immunoblot. Using polyclonal antibodies, the major portion of COMP from fibroblasts and culture supernatants was present as low-molecular-weight (LMW) bands, corresponding to those found in synovial fluids. These LMW COMP bands, however, were not detected in any of the cells or tissues tested using 18-G3 mAb. In protein extracts from ***chondrocytes*** and in COMP purified from ***cartilage*** , these LMW bands could not be detected. In conclusion, the data suggest that

certain forms of COMP detected in synovial fluid are secreted from synovial fibroblasts and could be distinguished by specific assays from COMP secreted by ***chondrocytes*** .

L26 ANSWER 29 OF 45 MEDLINE DUPLICATE 25
ACCESSION NUMBER: 1999120530 MEDLINE
DOCUMENT NUMBER: 99120530 PubMed ID: 9923655
TITLE: Retention of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) and cell death in redifferentiated pseudoachondroplasia ***chondrocytes*** .
AUTHOR: Hecht J T; Montufar-Solis D; Decker G; Lawler J; Daniels K; Duke P J
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical School at Houston, 77225, USA.
SOURCE: MATRIX BIOLOGY, (1998 Dec) 17 (8-9) 625-33.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 20020124
Entered Medline: 19990413

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) is a large extracellular glycoprotein that is found in the territorial matrix surrounding ***chondrocytes*** . Two skeletal dysplasias, pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (EDM1) are caused by mutations in the calcium binding domains of COMP. In this study, we identified two PSACH mutations and assessed the effect of these mutations on redifferentiated ***chondrocyte*** structure and function. We confirmed, in vitro, that COMP is retained in enormous cisternae of the rough endoplasmic reticulum (rER) and relatively absent in the PSACH matrix. The rER accumulation may compromise ***chondrocyte*** function, leading to ***chondrocyte*** death. Moreover, while COMP appears to be deficient in the PSACH matrix, the matrix appeared to be normal but the over-all quantity was reduced. These results suggest that the abnormality in linear growth in PSACH may result from decreased ***chondrocyte*** numbers which would also affect the amount of matrix produced.

L26 ANSWER 30 OF 45 MEDLINE DUPLICATE 26
ACCESSION NUMBER: 1999275245 MEDLINE
DOCUMENT NUMBER: 99275245 PubMed ID: 10343777
TITLE: Production of cartilage oligomeric matrix protein (COMP) by cultured human dermal and synovial fibroblasts.
AUTHOR: Dodge G R; Hawkins D; Boesler E; Sakai L; Jimenez S A
CORPORATE SOURCE: Department of Medicine, Thomas Jefferson University, Philadelphia, PA 19107, USA.
CONTRACT NUMBER: AR-39740 (NIAMS)
AR-42417 (NIAMS)
SOURCE: OSTEOARTHRITIS AND CARTILAGE, (1998 Nov) 6 (6) 435-40.
Journal code: 9305697. ISSN: 1063-4584.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990628
Last Updated on STN: 19990628
Entered Medline: 19990614

AB OBJECTIVE: ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) is a large disulfide-linked pentameric protein. Each of its five subunits is approximately 100,000 Da in molecular weight. COMP was originally identified and characterized in ***cartilage*** and it has been considered a marker of ***cartilage*** metabolism because it is currently thought not to be present in other joint tissues, except for tendon. To confirm the tissue specificity of COMP expression we examined cultured human dermal fibroblasts, human foreskin fibroblasts, and normal human synovial cells for the synthesis of COMP in culture. METHOD: Normal synovial cells and normal human dermal foreskin fibroblasts were isolated from the corresponding tissues by sequential enzymatic digestions and cultured in media containing 10% fetal bovine serum until confluent. During the final 24 h of culture, the cells were labeled with 35S-methionine and 35S-cysteine in serum- and cysteine/methionine-free medium. The newly synthesized COMP molecules were immunoprecipitated from

the culture media with a COMP-specific polyclonal antiserum, or with monoclonal antibodies or affinity-purified COMP antibodies. The immunoprecipitated COMP was analyzed by electrophoresis in 5.0% polyacrylamide gels. For other experiments, synovial cells cultured from the synovium of patients with rheumatoid arthritis (RA) and osteoarthritis (OA) were similarly examined. RESULTS: A comparison of the amounts of COMP produced by each cell type (corrected for the DNA content) revealed that synovial cells produced > or = 9 times more COMP than ***chondrocytes*** or dermal fibroblasts. COMP could be easily detected by immunoprecipitation in all cell types. Electrophoretic analysis revealed a distinct band with an apparent MW of 115-120 kDa in samples from each of the three cell types, regardless of the antibody used. COMP expression in cultures of synoviocytes derived from OA and RA patients showed that OA and RA synovial cells produced similar amounts of monomeric COMP of identical size to those COMP monomers produced by normal synovial cells. The addition of TGF-beta to these cultures resulted in an increase in COMP production in normal, OA and RA synovial cells (45, 116 and 115% respectively). CONCLUSION: These studies demonstrate that substantial amounts of COMP are produced by several mesenchymal cells including synoviocytes and dermal fibroblasts. These findings raise important concerns regarding the utility of measurements of COMP levels in serum or in synovial fluid as markers of articular ***cartilage*** degradation because of the likelihood that a substantial proportion of COMP or COMP fragments present in serum or synovial fluid may be produced by cells other than articular ***chondrocytes*** .

L26 ANSWER 31 OF 45 MEDLINE DUPLICATE 27
ACCESSION NUMBER: 1998420391 MEDLINE
DOCUMENT NUMBER: 98420391 PubMed ID: 9749943
TITLE: Characterization of cartilage oligomeric matrix protein (COMP) in human normal and pseudoachondroplasia musculoskeletal tissues.
AUTHOR: Hecht J T; Deere M; Putnam E; Cole W; Vertel B; Chen H; Lawler J
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical School at Houston, 77225, USA.
CONTRACT NUMBER: HL 49081 (NHLBI)
SOURCE: MATRIX BIOLOGY, (1998 Aug) 17 (4) 269-78.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981124
AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), the fifth member of the -thrombospondin gene family, is an extracellular matrix calcium-binding protein. The importance of COMP is underscored by the finding that mutations in COMP cause the human dwarfing condition, pseudoachondroplasia (PSACH). Here, we report the results of human tissue distribution and cell secretion studies of human COMP. COMP is expressed and secreted by cultured monolayer ***chondrocyte*** , tendon and ligament cells, and COMP secretion is not restricted to a differentiated ***chondrocyte*** phenotype. Whereas COMP is retained in the endoplasmic reticulum that accumulates within PSACH ***chondrocytes*** in vivo, COMP is not retained intracellularly in the dedifferentiated PSACH ***chondrocytes*** in cultures. These results lend further support to the hypothesis that retention of COMP is related to the terminal PSACH ***chondrocyte*** phenotype, processing of proteins related to extracellular matrix formation, and maintenance in ***cartilage*** .

L26 ANSWER 32 OF 45 MEDLINE DUPLICATE 28
ACCESSION NUMBER: 1998049569 MEDLINE
DOCUMENT NUMBER: 98049569 PubMed ID: 9388247
TITLE: The fate of cartilage oligomeric matrix protein is determined by the cell type in the case of a novel mutation in pseudoachondroplasia.
AUTHOR: Maddox B K; Keene D R; Sakai L Y; Charbonneau N L; Morris N P; Ridgway C C; Boswell B A; Sussman M D; Horton W A; Bachinger H P; Hecht J T
CORPORATE SOURCE: Research Department, Shriners Hospital for Children, Portland, Oregon 97201, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Dec 5) 272 (49) 30993-7.

Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United State[redacted]
DOCUMENT TYPE: Journal; Artic[redacted]e; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980122
Last Updated on STN: 19990129
Entered Medline: 19980108

AB We have identified a novel missense mutation in a pseudoachondroplasia (PSACH) patient in one of the type III repeats of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP). Enlarged lamellar rough endoplasmic reticulum vesicles were shown to contain accumulated COMP along with type IX ***collagen*** , a ***cartilage*** -specific component. COMP was secreted and assembled normally into the extracellular matrix of tendon, demonstrating that the accumulation of COMP in ***chondrocytes*** was a cell-specific phenomenon. We believe that the intracellular storage of COMP causes a nonspecific aggregation of ***cartilage*** -specific molecules and results in a ***cartilage*** matrix deficient in required structural components leading to impaired ***cartilage*** growth and maintenance. These data support a common pathogenetic mechanism behind two clinically related chondrodysplasias, PSACH and multiple epiphyseal dysplasia.

L26 ANSWER 33 OF 45 MEDLINE DUPLICATE 29
ACCESSION NUMBER: 97307954 MEDLINE
DOCUMENT NUMBER: 97307954 PubMed ID: 9164830
TITLE: Ultrastructural immunolocalization of cartilage oligomeric matrix protein (COMP) in porcine growth cartilage.
AUTHOR: Ekman S; Reinholt F P; Hultenby K; Heinegard D
CORPORATE SOURCE: Department of Pathology, Swedish University of Agricultural Science, Box 7028, S-750-07 Uppsala, Sweden.
SOURCE: CALCIFIED TISSUE INTERNATIONAL, (1997 Jun) 60 (6) 547-53.
Journal code: 7905481. ISSN: 0171-967X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970721
Last Updated on STN: 19990129
Entered Medline: 19970710

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) is a macromolecule of yet unknown function with restricted distribution among tissues. In the present study, the ultrastructural localization of COMP in porcine immature joint ***cartilage*** and growth plate ***cartilage*** was semiquantitatively delineated. Tissues were fixed in a mixture of low concentration glutar- and paraformaldehyde, embedded at low temperature, and subjected to immunocytochemistry using polyclonal antibodies raised against bovine COMP. Protein A-coated colloidal gold was used for detection. The most intense immunolabeling for COMP was noted in the proliferative zones of the growth ***cartilages*** . Here the concentration of immunomarker was higher in the territorial compartment than in the pericellular and interterritorial areas. A low concentration of COMP was observed in the resting and hypertrophic zones. The immunolabeling for COMP did not differ between the three matrix compartments of these zones. Supported by previous data obtained by in situ hybridization, the concentration of immunolabeling in the proliferative zone indicates a high rate of COMP synthesis in proliferative ***chondrocytes*** . Hence, COMP may be considered as a marker for normal differentiation into proliferative ***chondrocytes*** .

L26 ANSWER 34 OF 45 MEDLINE DUPLICATE 30
ACCESSION NUMBER: 97332434 MEDLINE
DOCUMENT NUMBER: 97332434 PubMed ID: 9188668
TITLE: Mosaicism in pseudoachondroplasia.
AUTHOR: Ferguson H L; Deere M; Evans R; Rotta J; Hall J G; Hecht J T
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical School at Houston, 77225-0708, USA.
SOURCE: AMERICAN JOURNAL OF MEDICAL GENETICS, (1997 Jun 13) 70 (3) 287-91.
Journal code: 7708900. ISSN: 0148-7299.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970724
Last Updated on STN: 19990129
Entered Medline: 19970715

AB Pseudoachondroplasia (PSACH) is a spondylo-epi-metaphyseal dysplasia characterized by disproportionate short stature, generalized ligamentous laxity, and precocious osteoarthritis. PSACH is caused by mutations in the ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) gene, which codes for a noncollagenous protein expressed in the territorial matrix of ***chondrocytes*** . Autosomal dominant inheritance has been demonstrated in many families; however, autosomal recessive inheritance has been suggested in some severe familial cases. Alternatively, germline/somatic mosaicism has been proposed and is credible, since it has been shown that dominantly inherited and sporadic cases of PSACH are caused by the same genetic defect. Here, we present evidence demonstrating somatic mosaicism in two PSACH families that were originally considered to represent autosomal recessive inheritance. The results of this study suggest that autosomal recessive inheritance is unlikely and all cases of PSACH should be studied for mutations in COMP.

L26 ANSWER 35 OF 45 MEDLINE DUPLICATE 31
ACCESSION NUMBER: 97400236 MEDLINE
DOCUMENT NUMBER: 97400236 PubMed ID: 9257730
TITLE: Expression of cartilage oligomeric matrix protein by human synovium.
AUTHOR: Di Cesare P E; Carlson C S; Stollerman E S; Chen F S; Leslie M; Perris R
CORPORATE SOURCE: Musculoskeletal Research Center, Hospital for Joint Diseases Orthopaedic Institute, New York, NY 10003, USA.. PEDiCesare@aol.com
CONTRACT NUMBER: RR08562 (NCRR)
SOURCE: FEBS LETTERS, (1997 Jul 21) 412 (1) 249-52.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970922
Last Updated on STN: 19990129
Entered Medline: 19970905

AB Human synovium was analyzed for the possible expression of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP). Immunostaining with polyclonal antiserum to COMP demonstrated positive staining within the synovial cells and immediately subjacent connective tissue, with less intense staining in the deeper connective tissue. Western blot analysis using either polyclonal or monoclonal antibodies to human COMP confirmed the presence of COMP by immunoreactive bands with the same molecular mass (approximately 110 kDa) as purified articular ***cartilage*** COMP. PCR using oligonucleotides that span human COMP exons 7-13 revealed identical amplification products from cDNA prepared from either human ***chondrocytes*** or synovium. Northern blot analysis using a biotinylated-probe to human COMP, spanning exons 12-13, also reveal an identical hybridization product to either human ***chondrocyte*** or synovium total RNA. Human synovium should be considered as a potential tissue source of COMP in any investigation of biological markers of ***cartilage*** metabolism.

L26 ANSWER 36 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 96:745291 SCISEARCH
THE GENUINE ARTICLE: VH883
TITLE: REGULATION OF ***CARTILAGE*** ***OLIGOMERIC*** ***MATRIX*** ***PROTEIN*** (COMP) SYNTHESIS IN HUMAN SYNOVIAL-CELLS AND ARTICULAR ***CHONDROCYTES***
AUTHOR: RECKLIES A D (Reprint); BAILLARGEON L; WHITE C
CORPORATE SOURCE: MCGILL UNIV, MONTREAL, PQ, CANADA
COUNTRY OF AUTHOR: CANADA
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1996) Vol. 39, No. 9, Supp. S, pp. 1462.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L26 ANSWER 37 OF 45 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1996:502068 BIOSIS
DOCUMENT NUMBER: PREV19969922[redacted]4
TITLE: Regulation of cartilage oligometric matrix protein (COMP) synthesis in human synovial cells and articular chondrocytes.
AUTHOR(S): Recklies, Anneliese D.; Baillargeon, Linon; White, Chantal
CORPORATE SOURCE: McGill Univ., Montreal Canada
SOURCE: Arthritis & Rheumatism, (1996) Vol. 39, No. 9 SUPPL., pp. S271.
Meeting Info.: 60th National Scientific Meeting of the American College of Rheumatology and the 31st National Scientific Meeting of the Association of Rheumatology Health Professionals Orlando, Florida, USA October 18-22, 1996
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L26 ANSWER 38 OF 45 MEDLINE DUPLICATE 32
ACCESSION NUMBER: 96228679 MEDLINE
DOCUMENT NUMBER: 96228679 PubMed ID: 8785592
TITLE: Distribution and expression of cartilage oligomeric matrix protein and bone sialoprotein show marked changes during rat femoral head development.
AUTHOR: Shen Z; Heinegard D; Sommarin Y
CORPORATE SOURCE: Department of Cell and Molecular Biology, University of Lund, Sweden.
SOURCE: MATRIX BIOLOGY, (1995 Dec) 14 (9) 773-81.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19961008
Last Updated on STN: 19990129
Entered Medline: 19960924

AB Distribution and sites of synthesis of a ***cartilage*** extracellular matrix protein, ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), and of a bone extracellular matrix protein, bone sialoprotein (BSP), were studied in the femoral head of growing Wistar rats from day 14 to day 60 by immunocytochemistry and in situ hybridization. This period includes formation of the secondary ossification center and differentiation of articular ***cartilage*** . At early stages, immunoreactivity for COMP was pronounced throughout the ***cartilage*** . The localization of COMP was predominantly territorial in the center of the immature femoral head and in the growth plate at all ages studied. In the superficial parts, a shift from a uniform extracellular matrix staining at day 14 to an interterritorial localization at day 33 to day 60 was seen, apparently concurrent with formation of articular ***cartilage*** . COMP staining, representing ***cartilage*** remnants, also extended into the center of the trabecular bone in the primary spongiosa. In the secondary ossification center, the staining for COMP decreased at the onset of calcification. The protein was only synthesized by ***chondrocytes*** , as shown by in situ hybridization. The highest level of COMP mRNA was detected in ***chondrocytes*** in the central region of the growth plate. In the layer corresponding to the articular ***cartilage*** of the femoral head, mRNA levels for COMP were low from day 14 to day 33 but were increased on day 60. This shows substantial synthesis in the developing articular ***cartilage*** . Immunoreactivity for BSP was detected in bone trabeculae of primary spongiosa. In situ hybridization showed the highest levels of BSP mRNA in regions of newly formed bone. BSP mRNA was detected in hypertrophic ***chondrocytes*** in the secondary ossification center as early as day 18, well before the appearance of immunochemically detectable BSP. Interestingly, simultaneous expression of COMP and BSP mRNA was seen after day 18 in hypertrophic ***chondrocytes*** of the growth plate and later also in hypertrophic ***chondrocytes*** close to the mineralization zone of the articular ***cartilage*** .

L26 ANSWER 39 OF 45 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:29371 CAPLUS
DOCUMENT NUMBER: 124:113431
TITLE: Distribution and expression of cartilage oligomeric matrix protein and bone sialoprotein show marked changes during rat femoral head development

AUTHOR(S): Shen, Zhenxin; Heinegaard, Dick; Sommarin, Yngve
CORPORATE SOURCE: Dep. Ce[redacted]Mol. Biology, University Lund, [redacted]nd, Swed.
SOURCE: Matrix Biology (1995), 14(9), 773=81
CODEN: MTBOEC; ISSN: 0945-053X
PUBLISHER: Fischer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Distribution and sites of synthesis of a ***cartilage*** extracellular matrix protein, ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), and of a bone extracellular matrix protein, bone sialoprotein (BSP), were studied in the femoral head of growing Wistar rats from day 14 to day 60 by immunocytochem. and in situ hybridization. This period includes formation of the secondary ossification center and differentiation of articular ***cartilage*** . At early stages, immunoreactivity for COMP was pronounced throughout the ***cartilage*** . The localization of COMP was predominantly territorial in the center of the immature femoral head and in the growth plate at all ages studied. In the superficial parts, a shift from a uniform extracellular matrix staining at day 14 to an interterritorial localization at day 33 to day 60 was seen, apparently concurrent with formation of articular ***cartilage*** . COMP staining, representing ***cartilage*** remnants, also extended into the center of the trabecular bone in the primary spongiosa. In the secondary ossification center, the staining for COMP decreased at the onset of calcification. The protein was only synthesized by ***chondrocytes*** , as shown by in situ hybridization. The highest level of COMP mRNA was detected in ***chondrocytes*** in the central region of the growth plate. In the layer corresponding to the articular ***cartilage*** of the femoral head, mRNA levels of COMP were low from day 14 to day 33 but were increased on day 60. This shows substantial synthesis in the developing articular ***cartilage*** . Immunoreactivity for BSP was detected in bone trabeculae of primary spongiosa. In situ hybridization showed the highest levels of BSP mRNA in regions of newly formed bone. BSP mRNA was detected in hypertrophic ***chondrocytes*** in the secondary ossification center as early as day 18, well before the appearance of immunochem. detectable BSP. Interestingly, simultaneous expression of COMP and BSP mRNA was seen after day 18 in hypertrophic ***chondrocytes*** of the growth plate and later also in hypertrophic ***chondrocytes*** close to the mineralization zone of the articular ***cartilage*** .

L26 ANSWER 40 OF 45 MEDLINE DUPLICATE 33
ACCESSION NUMBER: 95325938 MEDLINE
DOCUMENT NUMBER: 95325938 PubMed ID: 7602403
TITLE: Cartilage oligomeric matrix protein: isolation and characterization from human articular cartilage.
AUTHOR: DiCesare P E; Morgelin M; Carlson C S; Pasumarti S; Paulsson M
CORPORATE SOURCE: Cartilage and Bone Research Center, Hospital for Joint Diseases Orthopaedic Institute, New York, New York 10003, USA.
CONTRACT NUMBER: RR08562 (NCRR)
SOURCE: JOURNAL OF ORTHOPAEDIC RESEARCH, (1995 May) 13 (3) 422-8. Journal code: 8404726. ISSN: 0736-0266.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950822
Last Updated on STN: 19990129
Entered Medline: 19950809

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** was purified in a native form from normal adult human articular ***cartilage*** . The key steps in the purification scheme were selective extraction with buffer containing EDTA, wheat germ agglutinin affinity chromatography, and removal of the related protein thrombospondin by heparin affinity chromatography. Particles of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** viewed by electron microscopy after rotary shadowing revealed structures similar to the prototype molecule purified from Swarm rat chondrosarcoma. The protein demonstrated a bouquet-like five-armed structure, with peripheral globular domains connected by thin flexible strands to a central assembly domain. Immunohistochemistry revealed age-dependent differences in the protein's distribution in ***cartilage*** . In normal human adult articular ***cartilage*** , there was a relatively uniform distribution throughout the interterritorial extracellular matrix, whereas in fetal articular ***cartilage*** , immunostaining was localized to the extracellular

matrix directly adjacent to the ***chondrocytes*** . The isolation and characterization of human ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** will facilitate its study in pathological conditions of human ***cartilage*** .

L26 ANSWER 41 OF 45 MEDLINE DUPLICATE 34
ACCESSION NUMBER: 94333398 MEDLINE
DOCUMENT NUMBER: 94333398 PubMed ID: 8055970
TITLE: ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** and thrombospondin 1. Purification from articular ***cartilage*** , electron microscopic structure, and ***chondrocyte*** binding.
AUTHOR: DiCesare P E; Morgelin M; Mann K; Paulsson M
CORPORATE SOURCE: Cartilage and Bone Research Center, Hospital for Joint Diseases Orthopaedic Institute, New York, NY 10003.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1994 Aug 1) 223 (3) 927-37.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19940920
Last Updated on STN: 19990129
Entered Medline: 19940915
AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) and thrombospondin 1 (TSP1) were purified in a native form from normal bovine articular ***cartilage*** . The key step in the purification scheme was selective extraction with EDTA-containing buffer. Final separation of these two molecules was achieved by heparin affinity chromatography. Particles viewed by electron microscopy after rotary shadowing and negative staining revealed structures similar to their prototype molecules; from the Swarm rat chondrosarcoma for COMP, or from platelets for TSP1. Attachment of primary bovine ***chondrocytes*** to purified matrix proteins was investigated. Cells attached to COMP but not to the structurally related TSP1 indicating separate functions for these proteins in ***cartilage*** .

L26 ANSWER 42 OF 45 MEDLINE DUPLICATE 35
ACCESSION NUMBER: 95229140 MEDLINE
DOCUMENT NUMBER: 95229140 PubMed ID: 7713493
TITLE: Characterization of human and mouse cartilage oligomeric matrix protein.
AUTHOR: Newton G; Weremowicz S; Morton C C; Copeland N G; Gilbert D J; Jenkins N A; Lawler J
CORPORATE SOURCE: Division of Vascular Research, Brigham and Women's Hospital, Boston, Massachusetts 02115.
CONTRACT NUMBER: HL28749 (NHLBI)
HL49081 (NHLBI)
NO1-CO-74101 (NCI)
SOURCE: GENOMICS, (1994 Dec) 24 (3) 435-9.
Journal code: 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950524
Last Updated on STN: 19990129
Entered Medline: 19950518
AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) is a 524,000-Da protein that is expressed at high levels in the territorial matrix of ***chondrocytes*** . The sequences of rat and bovine COMP indicate that it is a member of the thrombospondin gene family. In this study, we have cloned and sequenced human COMP. Phylogenetic analysis using progressive sequence alignment and two parsimony-based algorithms indicates that the COMP gene and a precursor of the thrombospondin-3 and -4 genes were produced by a gene duplication that occurred 750 million years ago. An interspecific backcross mapping panel has been used to map the murine COMP gene to the central region of mouse chromosome 8. Southern blot analysis of a somatic cell hybrid DNA panel and in situ hybridization to human metaphase chromosomes indicate that the human COMP gene is located on chromosome 19 in band p13.1. These data confirm and extend the known regions of homology between human and mouse chromosomes and establish that COMP, like thrombospondin-1, -2, -3, and -4, is present in the human and mouse genomes.

L26 ANSWER 43 OF 45 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:422997 CAPLUS
DOCUMENT NUMBER: 119:22997
TITLE: COMP (cartilage oligomeric matrix protein) is structurally related to the thrombospondins
AUTHOR(S): Oldberg, Aake; Antonsson, Per; Lindblom, Karin; Heinegaard, Dick
CORPORATE SOURCE: Dep. Med. Physiol. Chem., Univ. Lund, Lund, S-221 00, Swed.
SOURCE: Journal of Biological Chemistry (1992), 267(31), 22346-50
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cloning and sequence anal. of cartilage oligomeric matrix protein (COMP) cDNA, representing a cartilage pentameric protein, revealed a protein of 755 amino acid residues with a calcd. mol. mass of 82,700 Da. Expression of the cDNA in COS cells showed that COMP is a homopolymer composed of five identical disulfide-linked subunits. COMP is homologous to the carboxyl-terminal half of thrombospondin, and the homologies include 89% and 54% of the residues in COMP and thrombospondin, resp. The similarities are most pronounced in the carboxy-terminal domains in which about 60% of the amino acid residues are identical. In the type 2/epidermal growth factor repeat domains the two proteins contain 41% identical residues. The sequence of the amino-terminal 84-amino acid residues is unique for COMP. Comparison of the amino acid sequences in the type 2 and type 3 repeat domains of COMP and the thrombospondins shows that COMP is the product of a unique gene and not the result of an alternatively spliced thrombospondin gene.

L26 ANSWER 44 OF 45 MEDLINE DUPLICATE 36
ACCESSION NUMBER: 92210585 MEDLINE
DOCUMENT NUMBER: 92210585 PubMed ID: 1556121
TITLE: Cartilage matrix proteins. An acidic oligomeric protein (COMP) detected only in cartilage.
AUTHOR: Hedbom E; Antonsson P; Hjerpe A; Aeschlimann D; Paulsson M; Rosa-Pimentel E; Sommarin Y; Wendel M; Oldberg A; Heinegard D
CORPORATE SOURCE: Department of Medical and Physiological Chemistry, University of Lund, Sweden.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Mar 25) 267 (9) 6132-6.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920515
Last Updated on STN: 19920515
Entered Medline: 19920504
AB An Mr = 524,000 oligomeric protein was isolated from bovine ***cartilage*** and designated COMP (***Cartilage*** ***Oligomeric*** ***Matrix*** ***Protein***). The protein is composed of disulfide-bonded subunits with an apparent Mr of 100,000 each. It is markedly anionic, probably due to its high contents of aspartic acid and glutamic acid, as well as to its substitution with negatively charged carbohydrates. COMP was found in all ***cartilages*** analyzed, but could not be detected in other tissues by enzyme-linked immunosorbent assay of guanidine HCl extracts. Within a given ***cartilage*** , COMP shows a preferential localization to the territorial matrix surrounding the ***chondrocytes*** .

L26 ANSWER 45 OF 45 MEDLINE DUPLICATE 37
ACCESSION NUMBER: 93079835 MEDLINE
DOCUMENT NUMBER: 93079835 PubMed ID: 1448898
TITLE: Immunohistochemical localization of matrix proteins in the femoral joint cartilage of growing commercial pigs.
AUTHOR: Ekman S; Heinegard D
CORPORATE SOURCE: Department of Anatomy and Histology, Swedish University of Agricultural Sciences, Uppsala.
SOURCE: VETERINARY PATHOLOGY, (1992 Nov) 29 (6) 514-20.
Journal code: 0312020. ISSN: 0300-9858.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930129
Last Updated on STN: 19930129
Entered Medline: 19921228

AB The immunocytochemical localization of several matrix macromolecules, including ***collagen*** type II and proteoglycans, in the distal femoral articular-epiphyseal ***cartilage*** complex of 15 commercial pigs between the age of 6 and 18 weeks was studied. Early osteochondrotic lesions, i.e., chondronecrosis in the resting region of the growth ***cartilage*** , as well as extensions of necrotic ***cartilage*** into the subchondral bone, were present in all animals, except those 6 weeks old. A battery of antibodies were used for identification of macromolecules in the matrix at different stages of the disease. ***Chondrocyte*** involvement in the process could be studied by identifying the sequence of alterations in matrix macromolecules as the lesion developed. The immunostaining for aggrecan (large aggregating proteoglycans), ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** , fibronectin, ***collagen*** type II, fibromodulin, and biglycan was more prominent in the areas of chondronecrosis, extending into the subchondral bone, than in the normal resting region. This altered pattern of matrix macromolecules resembled that of the matrix of the proliferative ***chondrocytes*** and suggests that the ***chondrocyte*** maturation had stopped in the proliferative zone. The matrix in the areas of chondronecrosis in the resting region resembled that in the normal resting region. Thus the chondronecrosis appears to have preceded alterations of the matrix composition. The antibody reactivity pattern was, however, altered in the matrix of the clustered ***chondrocytes*** in areas of chondronecrosis. Staining in these regions suggested a more prominent appearance of fibronectin and ***collagen*** type II than in the normal matrix of the resting region. These changes are suggestive of attempt to repair.(ABSTRACT TRUNCATED AT 250 WORDS)

=> d his

(FILE 'HOME' ENTERED AT 12:44:48 ON 07 JUN 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 12:45:12 ON 07 JUN 2003

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L1          1010 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5
L2         35062 S (50 KDA) OR (55 KDA) OR (62 KDA) OR (67 KDA)
L3             4 S L1 (P) L2
L4             1 DUPLICATE REMOVE L3 (3 DUPLICATES REMOVED)
L5             0 S L4 (P) TRYPSIN
L6            85 S HCOMP OR (HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROM
L7        261754 S ELISA
L8            93 S L7 AND L1
L9             6 S L6 AND L7
L10            2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)
L11          286 S L1 (P) (EXPRESS? OR RECOMBINANT)
L12           28 S L11 (P) CALCIUM
L13            6 DUPLICATE REMOVE L12 (22 DUPLICATES REMOVED)
L14            6 S L13 NOT (L4 OR L10)
L15           10 S L1 (P) PURIF? (P) CALCIUM
L16            2 DUPLICATE REMOVE L15 (8 DUPLICATES REMOVED)
L17       634480 S (BIOLOGICAL MATRIX) OR CARTILAGE OR (BONE MATRIX) OR COLLAGEN
L18         1001 S L1 (P) L17
L19           19 S L18 (P) COMPOSITION
L20            8 DUPLICATE REMOVE L19 (11 DUPLICATES REMOVED)
L21          140 S CALCIUM-REPLETE
L22            5 S L1 (P) L21
L23            1 DUPLICATE REMOVE L22 (4 DUPLICATES REMOVED)
L24        49652 S CHONDROCYTE OR (MESENCHYMAL STEM CELL) OR (DIFFERENTIATION AG
L25          181 S L18 (P) L24
L26           45 DUPLICATE REMOVE L25 (136 DUPLICATES REMOVED)
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=> log y

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